

The Relationship Between Rational Antibiotic Use and Therapeutic Outcomes in Patients with Community Acquired Pneumonia

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ARTICLE HISTORY:

Accepted : 2025-06-30

Published : 2025-06-30

KEYWORDS:

Antibiotics; Community acquired pneumonia; Gyssens Method; Rationality; Therapeutic outcomes

Citation:

Fortuna, T.A., Nuraini, F.R., Karuniawati, H. (2025). The Relationship Between Rational Antibiotic Use and Therapeutic Outcomes in Patients with Community Acquired Pneumonia. *Pharmacon: Jurnal Farmasi Indonesia*, 22(1), 84-91.
<https://doi.org/10.23917/pharmacon.v22i1.11678>

ABSTRACT

Pneumonia is an infection caused by microorganisms. Antibiotics are one of the treatments given to patients with pneumonia caused by bacterial infections. Rational use of antibiotics will prevent resistance. This study aims to determine the relationship between the rationality of antibiotic use and therapeutic outcomes in community-acquired pneumonia patients. We used a cross-sectional study and retrospectively collected data using purposive sampling. The inclusion criteria are non-ICU community pneumonia patients have complete medical record data, while the exclusion criteria are patients who died or had other infections. We evaluated the rationality of antibiotics using the Gyssens method. Based on the results, there are 240 patients, with 210 patients receiving rational therapy and 30 patients receiving irrational antibiotics. Based on the results, 6 patients did not receive antibiotics on time, 4 patients received the wrong dose, 2 patients did not get the correct interval, 16 patients received a dose that was too short, and 2 patients were prescribed alternative antibiotics that were more effective. The results of the analysis showed that there is a significant relationship between the rationality of antibiotic use and the therapeutic outcomes of community-acquired pneumonia patients (p-value < 0.001; OR 14.36).

INTRODUCTION

Pneumonia is a respiratory tract infection caused by microorganisms (viruses, bacteria, fungi, or parasites), in which the alveoli become filled with pus, making it difficult for the patient to breathe and limiting oxygen absorption (Indonesian Society of Respiriology, 2020). Community-acquired pneumonia is associated with high morbidity and mortality rates, particularly among elderly patients and those with comorbidities (PDPI, 2014). Common symptoms include cough, fever, and shortness of breath (Setiadi et al., 2022). According to the Indonesian Health Profile, pneumonia is one of the leading causes of death, with an incidence rate of 14.5% (Rumende et al., 2019).

One of the main therapies for pneumonia is antibiotic treatment, which is used to treat infections caused by microorganisms (Bestari & Karuniawati, 2019). Antibiotic administration

must be rational, as inappropriate use can negatively impact treatment outcomes. Irrational use of antibiotics can lead to resistance, reduced effectiveness, and increased side effects (Utsman & Karuniawati, 2020). According to a study by Sukriya (2020), 81.1% of patients received irrational antibiotic therapy. Similarly, Rahadjoputro (2023) reported that 93.34% of patients were given antibiotics irrationally. Rational use of antibiotics is essential to avoid treatment failure (Kristiani et al., 2019). The Gyssens method is a tool that can be used to evaluate the rationality of antibiotic use. A study by Hardiana et al. (2021) found that 28 patients received antibiotics rationally, while 15 did not. Another study by Widiyastuti (2023) showed that 72.91% of patients used antibiotics appropriately. Statistical analysis in the study showed a significant correlation between rationality and therapeutic outcomes (Widiyastuti et al., 2023). Based on several

studies, irrational antibiotic use remains prevalent, which encourages researchers to further investigate the issue. Therefore, this study is entitled "*The Relationship between the Rationality of Antibiotic Use and Therapeutic Outcomes in Patients with Community-Acquired Pneumonia.*"

METHODS

Study Design

This research is an observational study with a cross-sectional design. Data were collected retrospectively from patient medical records between January 2022 and December 2023. The collected data were analyzed using the chi-square test. This study received ethical approval from the Dr. Moewardi Hospital Ethics Committee with approval number 1.620/VIII/HREC/2023.

Population and Sample

The population in this study consisted of all adult patients diagnosed with community-acquired pneumonia. The sample in this study was patients who met the inclusion and exclusion criteria. A purposive sampling technique was used. Inclusion criteria were: patients diagnosed with non-ICU community-acquired pneumonia, aged over 18 years, and with complete medical record data. Exclusion criteria were: patients with other infectious diseases and patients who died. Based on calculations using the Slovin formula, the minimum required sample size for this study was 80 patients.

$$n = \frac{N}{1 + N(e)^2}$$

$$n = \frac{400}{1 + 400(0.1)^2} = 80$$

Description

n = Sample size

N = Size of population

E = Error tolerance limit (0.1)

Research Instrument

The instruments used in this study include the Gyssens flow diagram, the Indonesian Lung Doctors Association (PDPI) 2014 guideline, and the Guidebook for the Use of Prophylactic and Therapeutic Antibiotics at Hospital in Surakarta.

Data Analysis

We have analysed and presented the obtained data as tables with explanatory descriptions. We analysed medical record data using the chi-square test to determine the relationship between the rationality of antibiotic use and therapeutic outcomes.

Research Variables

The independent variable in this study is rationality, while the dependent variable is the patient's therapeutic outcomes. Patients in category 0 are rational; those in categories I-VI are irrational. In addition, it is said that there is a change in the patient's therapeutic outcomes, improving if the respiratory rate is <30/minute, the body temperature is normal, the symptoms disappear, and the leukocyte levels are <12,000/m³ (PDPI, 2014).

RESULT AND DISCUSSION

Patient characteristics

A total of 240 patients diagnosed with community-acquired pneumonia at the Regional Hospital in Surakarta during 2022-2023. The demographic characteristics of these patients are presented in **Table 1**. Based on the results of descriptive analysis, the number of community-acquired pneumonia patients was slightly higher in male patients (51.3%) compared to female patients (48.7%). The study's result aligns with Ilmi's research, which states that there are more male patients than female patients (60%). Male patients are more susceptible to pneumonia because they often engage in activities outside the home. On the other hand, lifestyle factors like smoking habits can cause this type of illness. Smoking can induce structural and functional changes in the respiratory tract and cilia, leading to inflammation and lung tissue damage, thereby increasing susceptibility to infections caused by microorganisms (Ilmi et al., 2020). Furthermore, smoking has been associated with a 1.5-fold increased risk of developing pneumonia compared to non-smoking, suggesting a potential link between tobacco exposure and respiratory tract infections (Jiang et al, 2020).

The majority of patients in this study (37.1%) were over 65 years old. Elderly patients are more susceptible to pneumonia because the immune system is already weakened

Table 1. Demographic characteristics of inpatient community-acquired pneumonia patients in 2022-2023.

Patient characteristics		Frequency	(%) n=240
Gender	Male	123	51.3
	Female	117	48.75
Age (Years)	17-25	11	4.6
	26-35	7	2.9
	36-45	22	9.2
	45-55	39	16.2
	56-65	72	30
	>65	89	37.1
Body Mass Index	Underweight	23	9.6
	Normoweight	120	50
	Overweight	55	22.9
	Obesity 1	28	11.6
	Obesity II	14	5.8
Comorbidities			
Without Comorbidities		54	22.5
With Comorbidities			
	Hipertension	83	34.6
	Renal Failure	28	11.6
	Diabetes mellitus	34	14.2
	Gastroesophageal Reflux	8	3.3
	Astma	4	1.6
	Anemia	7	2.9
	Stroke	6	2.5

(Kresnawati et al., 2021). These results align with Widyastuti's research, indicating that patients aged 65 and above dominate the pneumonia patient population. The complexity of clinical symptoms and faster disease progression in elderly patients puts patients at higher risk of developing pneumonia caused by multidrug-resistant (MDR) bacteria (Widyastuti et al., 2023).

Based on the patient's BMI (Body Mass Index), the results showed that the most dominant patients had a BMI range of 18.5-22.9 (120 patients). Patients with normal BMI have a higher chance of recovery compared to low BMI and obese patients. Weight loss in the overweight BMI group can accelerate the improvement of lung function and asthma control and improve quality of life (Leilani et al., 2023).

In addition to age, comorbidity is one of the determining factors in the severity of pneumonia. The study found that the most common comorbidity was hypertension, affecting 83 patients (34.6%). High blood pressure in hypertensive patients can cause changes in lung function, increasing susceptibility to pneumonia. The relationship between blood pressure and airway obstruction

has been demonstrated by a decrease in the FEV₁/FVC ratio (Zekafat et al., 2021). Therefore, people with hypertension are more susceptible to pneumonia (Nurhikmawati et al., 2020).

Antibiotic profile of community acquired pneumonia patients

Antibiotics for non-ICU inpatient community-acquired pneumonia patients consist of 7 antibiotics. These antibiotics are levofloxacin, ampicillin sulbactam, meropenem, ciprofloxacin, ceftriaxone, vancomycin, and ceftazidime. **Table 2** illustrates the distribution of antibiotic use. Levofloxacin was the most commonly prescribed antibiotic among the patients. As a fluoroquinolone, it is considered a preferred treatment option for individuals with pneumonia. This broad-spectrum antibiotic is often used as an initial empirical therapy prior to the availability of culture results and is also indicated for patients who do not respond to β -lactam antibiotics (Syahnar et al., 2021).

The antibiotics ampicillin-sulbactam, ciprofloxacin, ceftriaxone, and vancomycin are included in the administration of definitive antibiotics because they are administered after the patient's culture results are available. The definitive antibiotic most widely used by

patients is levofloxacin, with a percentage of 79.6%. These results align with Ilmi's (2020) findings, which indicated that levofloxacin was the most commonly prescribed antibiotic to patients at a rate of 62.71%. Levofloxacin was chosen because it is a broad-spectrum antibiotic that can be given to treat pneumonia caused by gram-positive and gram-negative bacteria (Ilmi et al., 2020).

Evaluation of the Rationality of Antibiotic Use Based on Gyssens' Flow Diagram

The appropriateness of antibiotic selection was assessed by the Gyssens flowchart, which assesses parameter suvhh as how complete the patient information is, how accurate the reasons for use are, the correct dosages, patient details, how the medicine is given, how often and how

Table 2. Profile of empirical and definitive antibiotic classification (n=240)

Antibiotic Categories	Antibiotic	Empirical Antibiotic	Definitive Antibiotic
Monotherapy Fluoroquinolones	Levofloxacin IV	191 (79.6%)	170 (70.8%)
	Moxifloxacin		1 (0.4%)
Beta lactam	Ampicillin sulbactam IV	8 (3.3%)	19 (7.9%)
Carbapenem	Meropenem IV	-	4 (1.6%)
Fluoroquinolones	Ciprofloxacin IV	3 (1.2%)	8 (3.3%)
Sefalosporine	Ceftriaxon IV	1 (0.4%)	5 (2.1%)
	Ceftadizim IV	-	2 (0.8%)
Combination			
Beta lactam + Macrolide	Ampicillin sulbactam IV + azithromycin IV	35 (14.6)	27 (11.2%)
Fluroquinolones+ vancomisin	Levofloxacin IV vancomycin IV	1 (0.4%)	2 (0.8%)
Beta lactam + vancomisin	Ampicillin sulbactam IV+ vancomycin IV	1 (0.4%)	1(0.4%)
Flouroquinolone+ betalactam	Levofloxacin IV+ meropenem IV	-	1 (0.4%)

IV: Intravenous

Furthermore, the antibiotics received by the patients were a combination of beta-lactam with macrolides (14.6%). The PDPI 2014 recommended this combination of antibiotics as the primary empirical treatment for non-ICU community pneumonia patients. In addition to the combination of beta-lactam with levofloxacin, patients also received a combination of levofloxacin with beta-lactam antibiotics (0.4%). Patients with risk factors for *Pseudomonas* receive this combination. Physicians prescribe meropenem to patients at risk of *pseudomonas* because of its broad-spectrum antipseudomonas properties in the lungs (Sari et al., 2017). For patients confirmed with MRSA, a combination of beta-lactam antibiotics with vancomycin (0.4%) and levofloxacin with vancomycin (0.8%) is given according to the 2014 PDPI guidelines. The main antibiotic used for MRSA is vancomycin, which works by blocking the building of the bacterial cell wall and can also change how the bacterial cell membranes work and affect the production of bacterial RNA (Pangestuti et al, 2020).

long the treatment lasts, and better and safer options. **Table 3** presents the evaluation results

The analysis found that the study's Gyssens flow diagram rated antibiotics' rationality at 87,5 % in category 0. In category 0, the use of antibiotics is considered rational when they are prescribed according to the patient's condition, have a broad spectrum, are safer and more effective, are administered in a timely manner, and involve the correct dose and route of administration. In the study, there were 210 patients who fell into category 0 with the use of fluoroquinolone antibiotics (levofloxacin) and beta-lactams as first-line therapy. These results are in line with research by Yusuf, where 84% of patients given levofloxacin antibiotics were in accordance with the 2014 PDPI guidelines (Yusuf et al., 2022).

In category IVA, there are more effective antibiotics than the ones used for the indication. Based on the results, there are two cases (1.3%) included in the IVA category with the use of ceftriaxone. The PDPI guidelines and hospital rules say that the best first antibiotic for treating

community-acquired non-ICU pneumonia is either a fluoroquinolone or a beta-lactam combined with macrolides. Patients in this IVA category receive a single dose of ceftriaxone (beta-lactam), based on data from the guidelines. According to Ilmi's research in 2020, it showed that levofloxacin as a first-line therapy is a broad-spectrum antibiotic that is superior to oral ceftriaxone and cefuroxime. Therefore, inappropriate use of antibiotics will affect the recovery of community-acquired pneumonia patients (Ilmi et al., 2020).

In category IIB, the administration of antibiotics was at an inappropriate interval. Gyssens recommends giving antibiotics at the same interval to maintain consistent drug levels in the blood. The results of the analysis obtained were two cases (1.3%) that fell into category IIB with the administration of ampicillin sulbactam and levofloxacin. According to the Guidelines, the recommended administration of levofloxacin is every 24 hours, but the patient was given it every 48 hours. The inappropriate administration of antibiotics resulted in the

Table 3. Antibiotic use of the Gyssens Category in CAP patients (n=240)

Rationality (Categories)	Antibiotic	Frequency	(%) n=240
Rational (0)	Levofloxacin	210	87.5
Irrational		30	
Inappropriate time (I)	Levofloxacin	6	2.5
Inappropriate dose (IIA)	Levofloxacin	4	1.6
Inappropriate interval (IIB)	Levofloxacin	1	1.3
	Ampicillin sulbactam	1	
Duration too short (IIIB)	Levofloxacin	16	10.4
	Ampicillin sulbactam		
There is a more effective alternative (IVA)	Ceftriaxone	2	1.3

In category I, the administration is inappropriate time. Based on the analysis, there were six cases (2.5%) included in category I with the use of levofloxacin antibiotics. In this case, the patient received 750 mg/24 hours of levofloxacin antibiotics given at 08.00 am, but on the second day, the patient was given antibiotics at 04.00 pm, so the time of administration was not appropriate. Inappropriate administration of antibiotics will cause drug levels in the blood not to always be the same, which will fail to achieve therapeutic effects in patients (Setiadi et al., 2022).

In category IIA, the administration of antibiotics was at an inappropriate dose. The results identified four cases (1.6%) in category IIA that involved the use of levofloxacin antibiotics. According to the guidelines (PDPI, 2014), the minimum daily dose is 500 mg, but the dosage given to the patient is 500 mg/48 hours. Dose adjustments can be made if the patient has liver and kidney dysfunction but the patient is not in this condition. Administering the right dose is crucial for the success of therapy. Incorrect dosing can cause the therapeutic effect on the patient not to be achieved, thus potentially causing therapy failure and the risk of side effects (Setiadi et al., 2022).

therapeutic effect not being achieved for the patient (Setiadi et al., 2022).

In category IIIB, the administration of antibiotics was too short. It is crucial to administer antibiotics at the appropriate time to prevent patients from developing resistance. The analysis revealed 16 cases (10.4%) classified as category IIIB. The patient was given the antibiotic levofloxacin 750 mg/24 hours, which was administered for only 2 days. The patient should have received empirical antibiotics for a minimum of 3 days. Antibiotics for too short a time will result in a decrease in drug levels in the body. They are insufficient to kill the microorganisms, which risks causing the therapeutic goal not to be achieved and resistance to occur (Tambun et al., 2019).

The relationship between the rational antibiotic use and therapeutic outcomes in CAP patients

The treatment provided aims to achieve optimal therapeutic outcomes in patients. Rational antibiotic use plays a critical role in ensuring the effectiveness of therapy. The results of the analysis are presented in Table 4. According to the results of the study, 103 patients received rational antibiotic use, and 19

Table 4. Relationship between Antibiotic Rationality and Therapy Outcomes in Community-Acquired Pneumonia Patients (n=240)

Rationality	Clinical Outcomes		Total	*P	OR	CI
	Improved	Not-improved				
Rational	194 (92.3%)	16 (7.4%)	210	< 0.001	14.361	1.09-1.23
Irrational	10 (33.3%)	20 (66.6%)	30			

patients received irrational therapy. A statistically significant association was found between the rational use of antibiotics and clinical outcomes ($p = < 0.001$). Patients who received irrational treatment were 14 times more at risk of therapeutic failure compared to patients who received rational treatment ($OR = 14.361$). These findings agree with earlier research by Asih Widyasuti, which found an association between appropriate antibiotic use and improved clinical outcomes in pneumonia patients (Widyasuti et al., 2023). In addition, there is also a study by Hardiana at RSPAD Gatot Subroto (p -value < 0.001) that shows a significant relationship between the rationality of treatment and patient therapy outcomes (Hardiana et al., 2021). Irrational use of antibiotics will have a negative impact, like bacterial resistance, which can increase the risk of side effects and therapy failure (Prakoso et al., 2018).

CONCLUSIONS

The most widely used antibiotic in this study was levofloxacin. Based on the results of the analysis using the Gyssens method, it was found that 214 patients received rational therapy and 30 patients received irrational therapy. The instances of irrationality identified in this study included 6 patients receiving antibiotics at the wrong time, 4 patients receiving the incorrect dose, 2 patients receiving antibiotics at the

wrong interval, 16 patients receiving their antibiotics for too short a duration, and 2 patients who had more effective antibiotic alternatives available. Based on the analysis, there are significant results between rationality and clinical outcomes ($p < 0.001$). Patients who received irrational treatment were 14 times more at risk of therapeutic failure compared to patients who received rational treatment.

ACKNOWLEDGMENT

We express our sincere gratitude to Muhammadiyah Research (Risetmu) for funding this study through the Regular Fundamental Research Scheme 1 Number 0258.503/I.3/D/2024.

AUTHORS' CONTRIBUTIONS

TAF: design study, review, editing, compilation of data, and supervision; HK: review and design study; FRN: design the study, collected sample, and writing the original draft

CONFLICT OF INTERESTS

The authors have no conflict of interest

ETHICAL CONSIDERATION

The authors certify that the work given in this article is original and that they accept any liability for claims related to its content.

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