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RATIONALITY OF ANTIBIOTICS PRESCRIBING IN COMMUNITY-ACQUIRED PNEUMONIA PATIENTS AT UNS HOSPITAL INPATIENTS UNIT IN 2021-2022

Erika Dyah Pramesti[1], Lusia Murtisiwi[1*], Truly Dian Anggraini[2]
[1]Bachelor Program of Pharmacy, Sekolah Tinggi Ilmu Kesehatan Nasional, Jl. Raya Solo-Baki, Kwarasan, Grogol, Sukoharjo, Central Java 57552, Indonesia
[2]Diploma III Program of Pharmacy, Sekolah Tinggi Ilmu Kesehatan Nasional, Jl. Raya Solo-Baki, Kwarasan, Grogol, Sukoharjo, Central Java 57552, Indonesia
*E-mail: lusia.murtisiwi@stikesnas.ac.id

Abstract

Community-acquired pneumonia (CAP) is the 3rd largest lower respiratory tract infection that causes death in the world. Treatment therapy that is generally used to treat pneumonia is by administering antibiotics. Irrational use of antibiotics can lead to less effective treatment, decreased drug safety, and increased resistance. This study aims to evaluate the rationality of using antibiotics in community-acquired pneumonia patients at UNS Hospital using the Gyssens method in 2021-2022. This research is a non-experimental research with a descriptive design and purposive sampling technique. Data collection was carried out retrospectively with a sample size of 19 patients who were hospitalized in 2021-2022. The data obtained were analyzed descriptively with the Gyssens assessment. The references used are Regulation of the Minister of Health Republic Indonesia Number 28, 2021 concerning Guidelines for the Use of Antibiotics, Guidelines for the Diagnosis of Community Pneumonia and Its Management in Indonesia 2014, UNS Hospital Drug Formulary, NICE Public Health Guidance 2022, and Dipiro 2020. The results of this study showed that 90.47% of patients received rational antibiotic therapy and 9.53% received irrational antibiotic therapy. Rational antibiotic therapy is an antibiotic that is included in category 0. The irrational use of antibiotics in this study is an antibiotic that is included in the IVC category (there are cheaper alternative antibiotics).
Keywords: Community-acquired pneumonia, antibiotics, Gyssens, rationality

INTRODUCTION

Pneumonia is an inflammation of the lungs caused by microorganisms such as bacteria, viruses, fungi and protozoa. Pneumonia has symptoms in the form of high fever accompanied by coughing up phlegm, fast breathing (breathing frequency > 50 times/minute), shortness of breath, and other symptoms (headaches, anxiety and decreased appetite)(Kemenkes RI, 2018). Pneumonia is a disease that infects approximately 450 million people per year and occurs all over the world. This disease is the leading cause of death in all groups, causing millions of deaths (7% of the world's total deaths) every year. According to the World Health Organization (WHO) which has stated that of the 10 types of diseases that cause death in the world, it is noted that lower respiratory tract infections are the 3rd largest infectious disease that causes death in the world. Pneumonia cases in Indonesia in community-acquired pneumonia requiring hospitalization are 20-40% and between these numbers 5-10% require intensive care. The prevalence rate of pneumonia requiring hospitalization in Indonesia is in the top 10 of all hospitalization cases. The highest case fatality rate (CFR) for pneumonia is 7.6% (Perhimpunan Dokter Paru Indonesia, 2014).

The initial therapy that can be used in the treatment of pneumonia is antibiotics. Irrational administration of antibiotics can increase the high level of antibiotic resistance, this can increase morbidity and mortality and will also increase health costs used by patients (Anita; Syamsul, 2019). Resistance is a health problem that must be managed worldwide because it causes an increase in mortality. Due to the increased development and spread of infections due to resistant microorganisms, in 2050 it is estimated that deaths due to antimicrobial resistance will be greater than deaths from cancer (Yulia et al., 2019).

This research supports the Antibiotic Resistance Control Program which is a government effort as a follow-up to the antibiotic control program proclaimed by the world health agency since 2011. Evaluation of the quality of antibiotic use is carried out to determine

the rationality of antibiotic use. Gyssens developed an evaluation of the use of antibiotics to assess the accuracy of the use of antibiotics which includes the accuracy of indications, the accuracy of selection based on effectiveness, toxicity, price and spectrum, duration of administration, dose, interval, route and time of administration. This research was conducted with the aim of knowing the percentage of rationality for using antibiotics in Community-Acquired Pneumonia (CAP) patients in inpatient installations at academic hospitals Sukoharjo in 2021-2022.

METHOD

This research was conducted using descriptive methods and retrospective data collection. The data taken is secondary data, namely the medical records of inpatient CAP patients in 2021-2022 obtained from an UNS hospital in Sukoharjo. This research has obtained permission in the form of Ethical Clearance (18/UN27.06.11/KEP/EC/2022). The sampling technique in this study was purposive sampling, which is a non-random sampling technique which meets certain criteria made by researchers based on the characteristics and characteristics of the population to be used. Inclusion criteria in the study were Community-Acquired Pneumonia patients who had complete medical record data, including: patient identity, date and time of examination, anamnesis results including at least complaints and medical history, results of physical examination and medical support, diagnosis, management plan, treatment and/or action, approval for action if needed, clinical observation notes and treatment results, discharge summary, doctor's name and signature. Exclusion criteria in this study were Community-Acquired Pneumonia patients who were referred, forced home, died and patients who had damaged/ilreadable medical record data. The total population of Community Acquired Pneumonia patients at the UNS Hospital Inpatient Installation in the 2021-2022 period was 22 patients, the sample included was 19 patients. A total of 3 patients were excluded because 1 patient was referred and 2 patients died.

The data obtained through medical records were then recapitulated in the Drug Therapy Monitoring (DTM) sheet, and then analyzed using the Gyssens method. Data analysis was carried out using the reference literature for the Regulation of the Minister of Health of the Republic of Indonesia Number 28 of 2021 concerning Guidelines for the Use of Antibiotics, Guidelines for the Diagnosis of Community Pneumonia and Its Management in Indonesia 2014, Formulary of Drugs for UNS Hospitals in Sukoharjo, NICE Public Health Guidance 2022, and Dipiro 2020. The results of the analysis of the use of antibiotics that fall into categories 0-6 were analyzed descriptively and presented in percentage form. Antibiotics are said to be rational if they are included in category 0.

RESULT AND DISCUSSION

There were 19 patients who were analyzed in this study. The results of this study recorded data on patient characteristics based on age and sex (table 1). The results of the analysis of the characteristics of CAP patients in the Inpatient Installation can be seen in table 1. This study shows that female patients are more dominant than male and the number of productive age patients (19-64 years) is greater than the number of geriatric patients (≥65 years). Lifestyle and environment are risk factors associated with CAP. This includes smoking habits, consuming alcohol, work and the work environment related to pollution levels and the level of density of the living environment. Other studies state that the incidence of CAP in passive smokers is greater than in active smokers (Almirall et al., 2017).

Table 1. Characteristics of patients Community Acquired Pneumonia in January 2021-December 2022 period

Characteristics	Number of patients	Percentage
Age (years)		
15-24	1	5,26
25-34	0	0
35-44	0	0
45-54	5	26,32
55-64	8	42,11
65-74	2	10,53
>74	3	15,79
Gender		
Female	12	63,16
Male	7	36,84
Total	**19**	**100**

Comorbidity is a condition in which a person suffers from two or more diseases at the same time. This can happen because people with comorbid diseases have a weaker immune system than people without comorbid diseases. The distribution of comorbidities in CAP patients at the academic hospital inpatient installation can be seen in table 2. The results of the analysis in table 2 show that 14.89% of patients have comorbid AKI (Acute Kidney Injury). Kidney disease is clearly known to be a risk factor for severe bacterial and viral infections, especially community-acquired pneumonia (Zasowski and Blackford, 2020). Renal disease patients have a pro-inflammatory status and functional defects in innate and acquired immune cells resulting in increased susceptibility to infection. In addition, there is an increased risk of pneumonia and upper respiratory tract infections in patients with kidney disease (Karya et al., 2021). Patients with comorbid renal impairment need to adjust the dose of the fluoroquinolone class of antibiotics because these drugs are nephrotoxic which can cause crystalluria and this can be avoided by adjusting the dose based on the patient's kidney function (Kemenkes RI, 2021).

Table 2. Distribution of comorbidities in Community Acquired Pneumonia patients in January 2021-December 2022 period

Comorbidities	Patient code	Number of comorbidities	Percentage
Stroke	A3, A18, A19	3	6,38
Hypertension	A1, A6, A7, A9, A14, A15, A19	7	14,89
UTI (Urinary Tract Infection)	A3, A17	2	4,26
COPD acute exacerbation	A2, A4, A11, A12, A16	5	10,64
AKI (Acute Kidney Injury)	A5, A6, A11, A12, A14, A15, A17	7	14,89
Asthma	A1, A7, A16	3	6,38
Diabetes Mellitus type II	A1, A5, A8, A11, A12, A15	6	12,77
CHF (Congestive Heart Failure)	A7, A8, A11, A12, A18	5	10,64
Dyslipidemia	A5, A14	2	4,26
Sepsis	A15, A17	2	4,26
ICHD (International Classification of Headcache)	A7	1	2,13
Anemia	A10	1	2,13
Hypokalemia	A3, A8, A10	3	6,38
Total		**47**	**100**

The antibiotic therapy used by Community-Acquired Pneumonia patients at the Inpatient Installation of UNS hospital in Sukoharjo can be seen in the table 3. The results of the analysis in table 3 show that 89.47% of patients received single therapy and 10.53% of patients

received combination therapy. These results are similar to the study by (Alfina, 2019) patients received 58% monotherapy and 42% dual therapy with antibiotics in community pneumonia. The most widely used antibiotics in this study were the third generation fluoroquinolones and cephalosporins. The aim of combination therapy is to increase the activity of antibiotics against specific infections, reducing and slowing the risk of emergence of resistant bacteria (Syahniar et al., 2021).

Table 3. Description of the use of antibiotics in patients with Community Acquired Pneumonia patients in January 2021-December 2022 period

Antibiotic Therapy	Number of antibiotics	Percentage
Single therapy	**17**	**89,47**
Levofloxacin IV	9	42,11
Seftriaxon IV	7	36,84
Azythromisin PO	1	5,26
Combination therapy	**2**	**10,53**
Levofloxacin IV + Seftriaxon IV + Azythromisin	1	5,26
Ampicillin Sulbactam IV	1	5,26
Total	**19**	**100**

The rationale for therapy in patients with Community-Acquired Pneumonia in the Inpatient Installation of an academic hospital in Sukoharjo studied in this study included the right indication, the right patient, the right dose, the right drug, evaluation of price and accuracy of drug administration in relation to the correct route of administration and duration of administration (Ihsan, 2021). Drug use must be rational to ensure patient safety by improving the patient's quality of life. The rationality of using antibiotics in Community-Acquired Pneumonia patients can be seen in table 4.

Table 4. The rationality of prescribing antibiotics based on the Gyssens method patients in January 2021-December 2022 period

Gyssens category	Number of Antibiotics	Percentage
Rational Category 0 (use of appropriate antibiotics)	19	90,47
Irrational IVC category (there are cheaper antibiotics)	2	9,53
Total	**21**	**100**

The medical records used as research material were selected for completeness of data through inclusion and exclusion criteria. The evaluated medical record data were complete so no antibiotic prescriptions were found in Community-Acquired Pneumonia patients who were included in category VI (patient medical records were incomplete and could not be evaluated). Antibiotics without indications can mean that antibiotic therapy is not needed for these patients. Signs and symptoms commonly found in pneumonia are fever, tachypnea, tachycardia, productive cough, and changes in sputum both in amount and characteristics. In addition, the patient will feel chest pain like being stabbed by a knife, inspiration is left behind by observing the rise and fall of the right chest when breathing (Perhimpunan Dokter Paru Indonesia, 2014). Assessment of the severity of community pneumonia can be done using a scoring system according to the Pneumonia Severity Index (PSI) or CURB-65. Levofloxacin IV antibiotics are adjusted to the Regulation of the Minister of Health of the Republic of Indonesia Number 28 of 2021 concerning Guidelines for the Use of Antibiotics, Guidelines for Community Pneumonia Diagnosis and Management in Indonesia 2014, Hospital Medicine Formulary and NICE Public Health Guidance 2022. Ceftriaxone IV antibiotics are adapted to the Home Medicine Formulary Hospital, IV ampicillin sulbactam and IV azithromycin were adjusted according to the 2020 UNS and Dipiro Hospital Medicine Formulary. The results of the analysis of antibiotic use using the Gyssens method, found no antibiotic prescriptions that were included in category V (antibiotic administration without indication).

Category IVA assesses the effectiveness of antibiotics from the therapeutic outcome to be achieved. Inappropriate selection of antibiotics can cause antibiotic resistance (Ihsan, 2021). A total of 19 patients analyzed in this study achieved the expected therapeutic outcomes. The therapeutic outcome is evidenced by clinical improvements through blood pressure, temperature, pulse, respiration rate and SPO2 (Perhimpunan Dokter Paru Indonesia, 2014). The summary of the patient who went home stated in the medical record stated that he had improved. The results of the analysis found no antibiotic prescription in pneumonia patients who were in the IVA category (there are other antibiotics that are more effective). The assessment of the IVB category is based on the need for antibiotic therapy with the patient's conditions such as contraindications, allergies and side effects that arise during therapy (Ihsan, 2021). The evaluation results found no antibiotic prescription in pneumonia patients who were in the IVB category (there are other antibiotics that are less toxic).

The IVC category is related to economic factors, namely drug prices, but not to pharmacoeconomic analysis which also takes into account other costs. The assessment of cheaper antibiotics was carried out on drugs of the same class within the same line of therapy. Price comparisons were made for the three drugs in the same group, not with the trade names of each drug, which of course is much more expensive (Ihsan, 2021). Cases A3 and A6 are in the IVC category (there are other antibiotics that are cheaper). Cases A3 and A6 received azithromycin antibiotic therapy which belongs to the macrolide group. Azithromycin is often given for indications of diseases such as community pneumonia, chronic bronchitis with acute exacerbations, sinusitis, urethritis, pelvic inflammatory disease, and other bacterial infections (Kirst, 2017). The price for azithromycin at UNS Hospital was IDR 1,476, while for erythromycin it was IDR 982. It can be concluded that Cases A3 and A6 fall into the IVC category, there is an antibiotic that is cheaper than azithromycin, namely erythromycin. According to the meta-analysis of Ashy et al., 2022, macrolides have antimicrobial activity against gram-positive bacteria such as Streptococcus pneumoniae, which is the most isolated organism associated with the pathogenesis of Community Acquired Pneumonia, as well as gram-negative bacteria such as Haemophilus influenzae, and atypical pathogens. However, erythromycin has limited activity against Haemophilus influenzae. Erythromycin and clarithromycin significantly inhibited CYP3A4 leading to increased levels of some drugs, while azithromycin had less drug-drug interactions. Although erythromycin is generally less expensive, clarithromycin and azithromycin have several advantages over erythromycin other than their activity against H. influenzae. They have a longer half-life than erythromycin and hence, their frequency of administration is low. In terms of safety, clarithromycin and azithromycin are considered as second generation macrolides which have a better side effect profile than first generation macrolides such as erythromycin.

The IVD category corresponds to more specific antibiotics with a narrower spectrum. The antibiotics evaluated in this study were given as empirical therapy aimed at eradicating or inhibiting the growth of bacteria suspected of being the cause of infection, before um the results of microbiological examination were obtained, so the antibiotics given were broad spectrum antibiotics. The selection of antibiotics with a narrow spectrum must be based on the results of blood cultures from the patient or based on local germ patterns (Ihsan, 2021). The antibiotics used in this antibiotic therapy are broad-spectrum antibiotics and their management is in accordance with the literature and drug formulary. The evaluation results found no antibiotic prescription in pneumonia patients included in the IVD category.

Category IIIA is related to taking antibiotics for too long. The use of antibiotics for too long, namely the administration of antibiotics for longer than the standard drug formulary used as a reference. According to the the longer the patient takes antibiotics, the greater the population of resistant bacteria because their development is not inhibited by commensal bacteria. The results of the evaluation did not find an antibiotic prescription that was included in category IIIA. Category IIIB regarding administration of antibiotics is too brief. The duration of using antibiotics differs, depending on the conditions experienced by the patient and the severity of the disease. The evaluation results found no antibiotic prescription in pneumonia patients who were in category IIIB.

Category IIA regarding the inappropriate dose of antibiotics. The dosage of antibiotics is inappropriate because the dose given to the patient exceeds the recommended dose or the dose given is less than the recommended dose. Too high a dose can cause toxic effects, while too low a dose may not produce the expected therapeutic effect (Syamsuni, 2016). Adequate

adjustment and optimization of doses and intervals of empiric antibiotic therapy in accordance with applicable guidelines is very important to achieve safe, effective and efficient treatment of infections. Patients with comorbid renal impairment need to make dose adjustments to fluoroquinolone antibiotics because these drugs are nephrotoxic which can cause crystalluria. (Vassalotti et al., 2016) in their review article stated that a reduction in the dose of fluoroquinolone class of antibiotics was required by 50% from the normal dose for conditions of glomerular filtration rate (GFR) <15 mL/min/1.73 m2. The Ministry of Health (2021) states that the initial dose of antibiotics is the same as the normal dose, then the dose is adjusted according to creatinine clearance, especially for antibiotics with a low therapeutic ratio. If the creatinine clearance is 40-60 ml/min, the maintenance dose is reduced by 50%. When the creatinine clearance is 10-40 ml/min and the dose is reduced by 50%, the dosing interval is doubled. Based on the results of the evaluation, there was no antibiotic prescription that was included in category IIA.

Category IIB related to the administration of antibiotics at inappropriate intervals. The interval for giving antibiotics is inappropriate, because the interval for giving is less or exceeds the interval suggested in the literature. The results of the evaluation found no antibiotic prescriptions included in category IIB. Category IB related route of administration. Route of administration is one indicator to assess the accuracy of a therapy. The route of drug administration must be chosen as the safest and most beneficial route for the patient (Kemenkes RI, 2021). Intravenous administration of antibiotics at the start of therapy is recommended for hospitalized community-acquired pneumonia patients because of the associated high mortality and the uncertainty of adequate absorption of oral antibiotics in seriously ill patients (Sukriya, Manggau, M. A. & Djaharuddin, 2022). The results of the evaluation did not find inappropriate antibiotic prescribing routes of administration of antibiotics. Category I related to inappropriate timing of antibiotics. The time of administration of antibiotics was evaluated at the time of administration every day. Timely administration of antibiotics is very important and can affect the outcome. A delay of 1 hour can reduce survival by almost 8% (Kurniati, A., Trisyani, Y. & Theresia, 2017). The results of the evaluation using the Gyssens method found no antibiotic prescriptions included in category I.

Category 0 concerns appropriate antibiotic prescribing. Antibiotic prescribing is called correct if it meets the criteria for the right diagnosis, the right indication of disease, the right choice of drug, the right dose, the right route of administration, the right interval for administration, the right duration of administration, alert to side effects, the right information and the right assessment of the patient's condition (Kemenkes RI, 2021). The total number of categories 0 was 19 antibiotics with a percentage of 90.47% of the total number of antibiotic prescriptions for Community-Acquired Pneumonia patients at the inpatient installation of UNS hospital in Sukoharjo in 2021-2022.

CONCLUSION

The results show that 90.47% of patients received rational antibiotic therapy (category 0) and 9.53% received antibiotic therapy irrational (IVC category there are cheaper alternatives).

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