Pharmaciana
Vol.12, No.1, July 2022, Page. 196-207
ISSN: 2088 4559; e-ISSN:.2477-0256
DOI: 10.12928/pharmaciana.v12i2.19242

Correlation of antibiotics prescribing appropriateness based on the pharmaceutical care network europe (PCNE) method and clinical response in Community-Acquired Pneumonia

Cut Fatia Ulfa[1], Woro Supadmi[1], Dyah Aryani Perwitasari[1*], Endang Yuniarti [2]
[1]Postgraduate Program of Faculty of Pharmacy, Universitas Ahmad Dahlan,
Jl. Prof.Dr.Soepomo S.H, Warungboto, Umbulharjo, Yogyakarta, Indonesia
[2]PKU Muhmamdiyah Hospital of Yogyakarta,
Jl. KH.Ahmad Dahlan No.22, Gondomanan, Yogyakarta, Indonesia

ABSTRACT

The use of antibiotics as the main standard of pneumonia treatment is usually prescribed in high quantities. Inappropriate selection of antibiotics can lead to bacterial resistance, treatment failure, and the emergence of DRPs (Drug-Related Problems). This study aims to determine the suitability of antibiotic prescribing using the PCNE method and to determine the correlation between the suitability of antibiotic prescribing and clinical response. This study was analyzed using a retrospective analytic cohort study method with data collection of adult Community-Acquired Pneumonia patients medical record, who were hospitalized in private hospital in Yogyakarta from January to December 2019. In addition, this study also assessed antibiotic prescribing according to the PCNE V8.02 method toward patients' clinical response (the number of leukocyte, temperature, and respiratory rate) after take the antibiotics. The correlation according to antibiotic prescribing analyzed according to chi-square method. The results showed that a total of 52 antibiotic regimens obtained in the evaluation of antibiotic prescribing according to the PCNE method were 21.5% suitable and 78.8% not suitable. Thus, the results of the correlation test for the accuracy of antibiotic prescribing and clinical response to the number of leukocytes showed a significant relationship ($p<0.05$). However in this study, none significant correlation was found in antibiotic prescription and clinical response in terms of temperature and respiratory rate ($p<0.05$).

Keywords: antibiotics prescribing appropriateness, PCNE, clinical response, community-acquired Pneumonia

Corresponding author:
Dyah Aryani Perwitasari
Postgraduate Program Faculty of Pharmacy, Universitas Ahmad Dahlan
Jl. Prof.Dr.Soepomo S.H, Warungboto, Umbulharjo, Yogyakarta, Indonesia
Email: dyah.perwitasari@pharm.uad.ac.id

INTRODUCTION

Community-Acquired Pneumonia is a form of acute inflammation of the lung parenchyma caused by germs (PDPI, 2014). Pneumonia is also an infectious disease and the third leading cause of death globally, with a death rate of 3.0 million from 15.2 million worldwide in 2016 (WHO, 2018). The Community-Acquired Pneumonia Organization (CAPO) reports the results of a cohort study on pneumonia mortality from 2001 to 2011 in North America, which accounted for 13.3%, 9.1% in Europe, and 7.3% in South America (Arnold et al., 2013). The United States also estimates that more than 1.5 million adult patients with CAP are hospitalized each year (Ramirez et al., 2017). In Indonesia, pneumonia is considered one of the top 10 infectious diseases. In 2013 the incidence of pneumonia had reached 1.6%, increasing to 2.0% in 2018. The fact shows an increase in the incidence of pneumonia (Riskesdas, 2018). The prevalence of pneumonia in the Special Region of Yogyakarta (DIY) at all ages is 18.06% (Indonesia Ministry of Health, 2019).

Community-Acquired Pneumonia is commonly caused by pathogenic bacteria, namely *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Streptococcus aureus, Legionella species, Chlamydia pneumoniae and Moraxella catarrhalis* (Metlay et al., 2019). The most common bacteria that cause CAP in Indonesia are *Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomortas aeruginosa* (Farida et al., 2015). The main standard treatment for CAP is the use of antibiotics which is repeatedly given to suspected pneumonia (Metlay et al., 2019 ; Klompas et al., 2020). However, improper use of antibiotics can lead to antibiotic resistance (Jenkins et al., 2012)

Antibiotic resistance has become a top threat to the public's health and a priority across the globe. It is estimated that there will be up to 10 million deaths due to infection by resistant bacteria per year in 2050 (WHO, 2014). Based on the results of the surveillance report on antibiotic resistance in Indonesia in 2018, the level of MRSA resistance to the antibiotic amikacin accounted for 80%, azithromycin was 60%, and ciprofloxacin was 45% (Dahesihdewi et al., 2019). The research results at Dr. Soeradji Tirtonegoro Klaten Hospital reported that the prevalence of MRSA continued to increase from 2015 to 2018, escalated from 7.69% to 5.63% to 10.85%, and 12.94% (Nuryah et al., 2019). Improper use of antibiotics can also lead to the length of stay, high medical costs, and DRPs. Antibiotic resistance can not be eliminated, but the use of appropriate antibiotics can prevent it; thus, antibiotic resistance can be overcome, and the burden of medical costs can be reduced (Ministry of Health , 2015).

Drug-Related Problems (DRPs) are an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. According to PCNE, the classification of DRPs can be grouped based on the problems and causes that are carried out in the case. DRPs based on problems are divided into several categories, namely effectiveness, security, and others. Besides, the causes-based DPRs include drug selection, drug dosage form, dosage, duration of treatment, drug delivery, how to use the drug, patient behavior, and others. This category system is used to facilitate the identification of DRPs that occur, thus they can be used as a measuring tool for evaluating drug therapy (Mil et al., 2017). Identifying DRPs using a category system enables us to provide an overview of the most common DRPs. Therefore, the decisions about which category has a severe impact on patients could easily be made (Campanelli et al., 2012).

According to a study conducted in China, identification of DRPs based on the PCNE classification of patients with Chronic Obstructive Pulmonary Disease (COPD) resulted in the incidence of DRPs at 54.2% of treatment safety, 24.2% of drug selection, 21.5% of dose selection, and 17.7% of treatment duration (Li et al., 2019). A study conducted at Fatmawati General Hospital in Jakarta from December 2014 through February 2015 also showed that the most frequent problem based on DRPs was the effect of not optimal drugs, which accounted for 80%. On the other hand, causes-based DRPs incidences that occurred were dose reduction (8%), low administration frequency (60%), and too high dose (12%)(Istita et al., 2020).

Evaluation of antibiotic use is an indicator of the quality of antibiotic resistance control programs in hospitals (Ministry of Health, 2015). The use of appropriate and controlled antibiotics can prevent the incidence of resistance, reduce the cost burden, and shorten the length of treatment

(Indonesia Ministry of Health, 2011). Community-acquired pneumonia patients usually show clinical response after antibiotic administration. Leukocyte count, temperature, and respiratory rate are clinical responses to the effectiveness of treatment (PDPI, 2014).

Based on the background of the study stated above, it is essential to conduct research to perceive the appropriateness of antibiotics prescribing based on the PCNE method and see the correlation of antibiotics prescribing appropriateness and clinical response in community-acquired pneumonia at a private hospital in Yogyakarta.

Methods

Research design and setting

This research is an analytic descriptive observational with a retrospective cohort design conducted retrospectively at a private hospital in the Yogyakarta area in January - December 2019. This research has received ethical approval from the Health Research Ethics Commission, Faculty of Health, University of Jendral Achmad Yani Yogyakarta with Number SKep / 02 / KEPK / II / 2020.

Research Data

The data of this research were obtained from patients' medical records including age, gender, diagnosis with ICD J.18.9, comorbidities, subjective data, objective data, and length of stay. Moreover, the empiric antibiotic therapy included the type of antibiotic, single-use dose, route of administration, frequency, and duration of administration. The evaluation of the appropriateness of antibiotics prescribing in this study was based on the PCNE method. The prescribing was considered appropriate when there was no DPRs incidence. On the other hand, it would be classified as inappropriate when there was a DPRs incidence. The treatment effectiveness was seen on the third day after antibiotic use. Treatment effectiveness parameters included the leukocyte count in which it classified as improved (4000-10,000/mm2) and not improved (<4000 or> 10,000 / mm2). Furthermore, the respiratory rate was assumed to be improved (≤24x / minute) and not improved (> 24x / minute). Lastly, the temperature was considered improved (36.0 - 37.8 ℃) and not improved (<36.0 or> 37.8 ℃). The study subjects were taken from all populations of community-acquired pneumonia patients in 2019. The inclusion criteria for the study subjects were medical records in male and female adult patients aged ≥ 18 years who were diagnosed with community pneumonia and used antibiotics during hospitalization.

Data Analysis

Data analysis was conducted descriptively for patient characteristics, antibiotic usage profile, and of antibiotic prescribing appropriateness based on the PCNE method and clinical response. Data in this research were presented in categorical and percentage form. Correlation of antibiotics prescribing appropriateness based on the pharmaceutical care network europe method and clinical response was analyzed using the Chi-square test. However, in case it was unable to comply with the requirements, Fisher exact would be used with a confidence interval (CI) of 95%.

Results and Discussion

Patient characteristics

This research was conducted at a private hospital in the Yogyakarta area of adult community-acquired pneumonia patients who were hospitalized in January - December 2019. 41 research subjects met the inclusion criteria. The research data were obtained from the patients' medical records. Patient characteristics in this study are presented in a descriptive form consisting of age, gender, comorbidities, and length of stay as shown in Table 1.

Table 1. Patient characteristics

Patient Characteristics	Total (n= 41) (%)
Age (Years)	
≤60	13(31.7)
>60	28(68.3)
Gender	
Male	21(51.2)
Female	20(48.8)
Length Of Stay (LOS)	Mean ±SD
Days	6.2±2.5
Patient Distribution	
Patients without comorbidities	13(31.7)
Patients with comorbidities	28(68.3)
Distribution of Comorbid Diseases in Patients	n = 39 (%)
Congestive Heart Failure (CHF)	6(15.4)
Diabetes Mellitus	5(12.8)
Hypertension	5(12.8)
Respiratory Failure	4(10.3)
CKD (Chronic Kidney Disease)	4(10.3)
Dyspepsia	3(7.7)
Hypokalaemia	3(7.7)
PPOK (Chronic Obstructive Pulmonary Disease)	2(5.1)
Asthma	2(5.1)
Stroke	1(2.6)
Anorexia	1(2.6)
Hyperthyroidism	1(2.6)
Back pain	1(2.6)
Epilepsy	1(2.6)

Table 1 showed the demographic and clinical data of the patients. The result showed that the majority of adult CAP patients were male (51.2%) compared to women (48.8%). The result of this research was in line with the previous study that reported that the gender characteristics of male patients were 74.5% and female were 25.5% (Faisal et al., 2014). The same result was also presented by Nie et al., (2018) of outpatients and inpatients of a hospital in China that male CAP patients were as much as 61.7% and female patients were 38.3%. In addition, Presley et al., (2015) published a result of their study claimed that the proportion of incidence of CAP in males was 56.25% and female was 43.75%.

Another result of this study showed that the majority of CAP patients were in the age group> 60 years (68.3%) and age ≤60 years (31.7%). The result of this research was in accordance with the previous research by Sari et al., (2017) which claimed that the highest incidence of pneumonia was found at patients whose age more than 60 years old. Older age is one of several risk factors of pneumonia (Mulyana, 2019).hence it is most often found in the elderly. This is due to the result of the aging process, decreased function of the body's cells, and also a function of the body's immune system so that degenerative diseases, malnutrition, and infectious diseases occur (Permenkes, 2015).

The result of this study also revealed that the average Lenght of Stay was 6,2±2,5 days. Similarly, n a study by Sudibyo, (2019) in PKU Muhammadiyah Gamping Hospital reported that the

average LOS in community-acquired pneumonia patients was 4.9 ± 1.6 days. Firmansyah et al., (2015) conducted a retrospective cohort study on adult patients diagnosed with CAP in RSCM (Dr. Cipto Mangunkusumo Hospital) in 2010-2014 reported an average length of stay of 8 days, with a minimum of 1 and a maximum length of stay of 63 days. Length of stay should be shortened to reduce treatment costs and prevent nosocomial infections (PDPI, 2014). In addition, the comorbidities were found in 28 patients (68.3%) namely 6 patients (15.4%) with Congestive Heart Failure (CHF) followed by diabetes mellitus and hypertension as much as 12.8%. Likewise, the same research conducted by Sari et al., (2017), stated that the highest comorbidities found in CAP patients were CHF (33.7%) and diabetes mellitus (30.1%). Comorbidity is an important determinant of the risk of pneumonia and affects the prognosis. In the study, CHF was the most common comorbidity. Heart failure will affect the function of the respiratory tract along with impaired cough reflex, impaired mucociliary clearance and ineffective coughing. This condition results in a delay in the appearance of clinical manifestations of pneumonia.

Antibiotic usage profile

Antibiotics are the standard treatment for pneumonia. The choice of antibiotic treatment for patients is individual, either single or in combination (Ministry of Health, 2011). The use of antibiotics in this study was empiric, no culture results were carried out. The profile of antibiotic usage in this study shown in Table 2.

Table 2. Antibiotic usage profile

Antibiotic	Total (%)
Antibiotic Therapy	41(100)
Single	30(73.2)
Combination	11 (26.8)
Antibiotic Classification	51(100)
Cephalosporin	33(63.5)
Fluoroquinolone	12(23.1)
Macrolide	6(11.5)
Others (Clindamycin)	1(1.9)
Types of Antibiotic	41(100)
Ceftriaxone	11 (26.8)
Ceftazidime	9(22.0)
Levofloxacin	6(14.6)
Ciprofloxacin	2 (4.9)
Cefepime	1 (2.4)
Cefotaxime	1 (2.4)
Ceftriaxone + Azithromycin	3 (7.3)
Ceftazidime + Azithromycin	3 (7.3)
Ceftazidime + Levofloxacin	2 (4.9)
Ceftriaxone + Levofloxacin	2 (4.9)
Ceftazidime + Clindamycin	1 (2.4)

Based on Table 2, shows that most of the single antibiotics were used in 30 patients (73.2%). Ceftriaxone was the most widely used antibiotic in community pneumonia patients as many as 11 patients (26.8%). Found in a previous study by Yulia et al., (2020) reported that in community pneumonia patients, the most widely used antibiotic was ceftriaxone (63.64%).

The results of the study reported by Islam et al., (2017) showed CAP patients, where the most widely used antibiotic was ceftriaxone 42.85%. Ceftriaxone, a beta-lactam antibiotic, is considered

effective against gram-positive and harmful bacteria. According to the Indonesian Lung Doctors Association (PDPI), the causes of community pneumonia in hospitalized are gram-negative bacteria such as Klebsiella pneumonia and gram-positive bacteria such as Streptococcus pneumonia. Beta-lactam monotherapy was rated as effective as a combination of beta-lactams and macrolides or fluoroquinolone monotherapy concerning 90-day mortality. The study results by Leyenaar et al., (2014) in pneumonia patients who received beta-lactam monotherapy, the combination of beta-lactams and macrolides did not show a significant difference in the length of hospitalization. Beta-lactam monotherapy can reduce hospital costs compared to the variety of beta-lactams and macrolides.

In this study, combination antibiotics were obtained as much as 26.8%. The most widely used combination antibiotic is a combination of beta-lactams (ceftriaxone, ceftazidime) and macrolides (azithromycin). This follows the recommendations from IDSA/ATS, which states that the treatment of non-ICU inpatients in adults can use beta-lactam antibiotics such as ceftriaxone ceftazidime combined with macrolides such as macrolides azithromycin (Mandell et al., 2007).

The appropriateness of antibiotics prescribing using the PCNE method

According to the Foundation Pharmaceutical Care Network Europe, DRPs is defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. DRPs can be classified based on problems, causes, and interventions for the case (Mil et al., 2017). In this study, the appropriateness of antibiotic prescribing evaluation was carried out by the PCNE method in which the DRPs classification that occurs is based on problems and causes. The results of evaluating the appropriateness of antibiotics prescribing by the PCNE method are presented in Table 3.

Table 3 presented the appropriateness of antibiotic prescribing based on the PCNE method. The data in Table 3 showed that there were 41 inappropriate regimens (78.8%) and 11 appropriate prescribing (21.2%) of the total 52 antibiotic regimens in CAP patients at a private hospital in the Yogyakarta area in January - December 2019 period. The most common DRPs incidence in the problem category was in the treatment effectiveness (P1) with a total of 31 prescriptions (64.6%). including the non-optimal effect of drug treatment (P1.2). In this study, the non-optimal therapeutic effect was seen after 3 days of antibiotic use. Where after using antibiotics for 3 days the patient's condition has shown clinical symptoms to improve and the number of leukocytes has decreased but has not reached normal. This is because the patient's condition at the time of admission to the hospital is different, such as the presence of co-morbidities that hinder the response to treatment of bacterial infections.

Another result of this study revealed that the incidence of DRPs in the cause category were dose selection (C3) as much as 6.3% and the duration of treatment (C4) which was 29.2%. The incidence of DRPs at dose selection (C3) was too high drug dose (C3.2). In this study, high doses were found in 3 prescribes using the levofloxacin antibiotic. Based on the Drug Information Handbook (DIH) the use of the levofloxacin antibiotic in patients with impaired kidney function was subject to dose adjustments. In addition, the incidence of DRPs in terms of the treatment duration occurred in 14 incidents (29.2%) including too short duration (C4.1) and too long duration (C4.2). The duration of antibiotics was too short in 13 patients, this was because the patient was able to be discharged after 3 days of being hospitalized. The clinical condition of the patient when he was discharged had improved but the laboratory results which stated that the patient's leukocyte count had not yet reached normal. Too long duration was found in one patient, this was because the patient had comorbidities. Based on (PDPI, 2014), the minimum use of antibiotics is 5 days and the duration of antibiotic use is 7-21 days based on treatment response and comorbidities.

Table 3. The incidence of DRPs based on the PCNE Method (n = 41)*

	The Appropriateness of Antibiotic Prescribing	Total **n=52(%)
	Appropriate	11(21.5)
	Inappropriate	41(78.8)
Code	DRPs Category	Total n=48(%)
	Problem	
P1	Treatment effectiveness	31(64.6)
P1.1	No effect of drug treatment/therapy failure	0
P1.2	Effect of drug treatment not optimal	31(64.6)
P1.3	Untreated symptoms or indication	0
P2	Treatment Safety	0
P2.1	Adverse drug event (possibly) occurring	0
	Cause	
C1	Drug Selection	0
C1.1	Inappropriate drug according to guidelines/formulary	0
C1.2	Inappropriate drug (within guidelines but otherwise contra-indicated)	0
C1.3	No indication for the drug	0
C1.4	Inappropriate combination of drugs (interaction with antibiotics)	0
C1.5	Duplication occurs	0
C2	Drug Form	0
C2.1	Inappropriate drug form	0
C3	Dose Selection	3(6.3)
C3.1	Drug dose too low	0
C3.2	Drug dose too high	3(6.3)
C3.3	Dosage regimen not frequent enough	0
C3.4	Dosage regimen too frequent	0
C4	Treatment Duration	14(29.2)
C4.1	Duration of treatment too short	13(27.1)
C4.2	Duration of treatment too long	1(2.1)

** means that there is a 51 rigemens; *41 subjects

A similar study conducted by Istita et al., (2020) on pneumonia patients in the inpatient care facility of the Fatmawati Central General Hospital, Jakarta, showed that there were 25 cases of DRPs occurred based on the PCNE V.6.2 analysis in which of the 30 patients, 18 patients experienced DRPs incidence with a total of 25 cases. In this case, 1 patient could experience more than 1 case of DRPs. Likewise, the same results of the study by Aulia, (2017) also presented the analysis of DPRs with the PCNE V.07 method with the following results; there were 36 causes with 19 causes in drug selection, no DRPs incidence in the selection of drug form and 2 DRPs in term of treatment duration.

In addition, the study conducted at the Turkish Hospital showed a potential DRPs incidence in 165 patients (80%) with a mean DRPs incidence of 1.6 / patient. The most common causes of DRP were inappropriateness in drug selection (44.78%), dose selection (27.61%), 1.23% drug form, and 1.84% duration of treatment (Abunahlah et al., 2018). Furthermore, Sneha et al.,(2019) found six types of identification of DRPs in 46 prescriptions, namely inappropriate drug (2), inappropriate dose (14), inappropriate frequency (5), drug interactions (28), therapeutic duplication, and (5), inappropriate indication (7).

Reported a study in a local government hospital in Jakarta on the Drug Related Problems (DRPs) assessment based on the Pharmaceutical Care Network Europe (PCNE) V.07 classification in

which problem and cause classification were assessed. The result of the study revealed that of the total subjects obtained from 100 patient medical records, there was 4 incidence of DRPs in term of treatment effectiveness and 4 problems of undesired drug reactions. On one hand, in the category of the cause, there were 36 causes with 19 causes related to drug selection, no causes were found related to the selection of drug form, 15 causes were related to dose selection, 2 causes were related to the length of treatment, and 30 causes were causes that had the potential to cause problems in the treatment effectiveness and undesired drugs reactions (Aulia, 2017).

Similarly, research conducted by Pramudya, (2020) on pneumonia in pediatric patients at UGM Academic Hospital which aimed to see an overview of potential DRPs patterns based on PCNE classification showed that there were 69 cases of DPRs incidence. The most common DRPs that occurred in problem classification were related to inappropriate drug combinations as many as 54 cases, 12 cases related to a too low dose, and 3 cases related to inappropriate drug selection (not according to guidelines/formulary). The results of a previous study by Sneha et al., (2019) on the evaluation of antibiotic prescribing in hospitalized patients showed that of all 46 prescriptions were found to be irrational and 214 prescriptions rational, irrationality was found mostly due to drug interactions.

Clinical response

Parameters of clinical response include leukocyte count, respiratory rate, and temperature. Clinical response can be seen from changes in the decrease in the value of each parameter before and after using antibiotics. The mean number of leukocytes before the use of antibiotics was 16,714 ± 6,089, while after using antibiotics for three days it was obtained (1.2024 ± 4.207). The mean respiratory frequency before 24.85 ± 7.67 and 21.49 + 4.12 after the use of antibiotics. The mean temperature value before (37.16+0.95) and after (36.73 ± 0.78). In this study, clinical response was seen after using antibiotics for three days.

Table. 4 Clinical response after the use of antibiotics

Clinical Response	Total (%)
Leukocyte Count	52 (100)
Improved	24(46.2)
Not improved	28(53.8)
Respiratory Rate	52 (100)
Improved	41(78.8)
Not improved	11(21.2)
Temperature	52 (100)
Improved	47(90.4)
Not improved	5(9.6)

Table 4 showed the frequency distribution of clinical response in CAP patients. Leukocyte count is a clinical response in CAP patients because the increase in leukocytes affects the severity and mortality of pneumonia patients (Blot et al., 2014). Clinical response parameters were measured based on leukocyte count. Table 4 showed that out of 52 regimens, 24 regimens (46.2%) did not improve and 28 regimens (53.8%) improved. Previous research conducted by Faisal et al., (2014) at the *Persahabatan* Hospital Jakarta in CAP patients showed a decreased number of leukocytes after antibiotics treatment from an average of 15,270 cells / mm3 to 12,000 cells / mm3 at the end of treatment which was in the fifth day after empiric antibiotics given. The increase in respiratory rate is commonly indicated by shortness of breath. Shortness of breath is a diagnosis of CAP (PDPI, 2014). The result of this study showed that patients, clinical response in terms of the respiratory rate was improved (78.8%) and not improved (21.2%). On the other hand, another clinical response parameter used in this study was measured by temperature. Clinical response is assumed to improve when the temperature is 36.0-37.8℃ and not improved when the temperature is > 37.8 ℃. In this study, with a

total of 52 regimens, 90.4% improved and 9.6% did not improve. Research conducted by Sari et al., (2017) revealed that the average temperature in CAP patients was 37.1 ℃. According to (PDPI, 2014), CAP patients are considered to be improved when they have no fever or the clinical condition is stable (temperature ≤37.8 ℃).

Evaluation of the antibiotics prescribing based on the PCNE method

Evaluation appropriateness of antibiotic prescribing using the PCNE method using the Sci-square test analysis to determine the correlation between the accuracy of antibiotic use and the success of therapy in community pneumonia patients. The results of the analysis of each parameter are presented in Table 5.

Table 5. Correlation of antibiotics prescribing appropriateness and clinical response

Clinical Outcome	Appropriateness of Antibiotics Prescribing	Clinical Response		*p*	RR	CI (95%)
		Improved	Not Improved			
Leukocytes	Appropriate	13	0	0.001*	3.54	2.14-5.85
	Inappropriate	11	28			
Respiratory Rate	Appropriate	11	2	0.70	1.65	0.30-8.86
	Inappropriate	30	9			
Temperature	Appropriate	13	0	0.31	1.14	1.01-1.29
	Inappropriate	34	5			

Note: * means that there is a significant relationship with p-value <0.05

p: p-value, RR: Risk ratio, CI: Confidence interval, analyzed using the Chi-square test

Table 5 presented the appropriateness of antibiotics prescribing based on the PCNE method and patients' clinical response. The data in Table 5 showed that there were 13 regimens with appropriate prescribing that resulted in improvement in leukocyte count and 11 regimens with inappropriate antibiotics prescribing also resulted in an improvement. In contrast, of all the inappropriate antibiotic prescribing, only 11 regimens resulted in an improved condition. The significant value indicates that there is a correlation of antibiotic prescribing to the clinical response on the leukocyte count parameter (p = 0.001; RR = 3.54; CI = 2.14-5.85). This implied that the appropriateness of antibiotic prescribing had a 3.54 times chance of improving clinical compared to inappropriate antibiotic prescribing.

In addition, the antibiotic prescription appropriateness based on the pharmaceutical care network europe method to clinical response in terms of respiratory rate showed that, of all the correct antibiotic prescriptions, only 11 regimens resulted in improvement. On one hand, of all the inappropriate antibiotic prescriptions, only 30 regimens were in an improved condition. Significant values indicated that there was no correlation between the appropriateness of antibiotics prescribing and clinical response in respiratory rate parameters (p = 0.70; RR = 1.65; CI = 0.30-8.86).

Moreover, the appropriateness of antibiotic prescribing based on the PCNE method to clinical response in terms of temperature showed that, of all the correct antibiotic prescriptions, only 13 regimens were in an improved condition. Meanwhile, of all the inappropriate antibiotic prescriptions, only 34 regimens resulted in an improved condition. The significant value showed no relationship between the appropriateness of antibiotic prescriptions and clinical response in temperature parameters (p = 0.31; RR = 1.14; IC95% = 1.01-1.29).

Abunahlah et al., (2018), reported that in a Turkish hospital there was no significant correlation between the incidence of DRPs and length of stay (p > 0.05). Similarly Aulia, (2017) also reported in her study that there was no correlation between length of stay and the incidence of DRPs (p > 0.05). Another study conducted by Pramudya, (2020) on pneumonia in a pediatric patient at the Gajah Mada University Academic Hospital showed that there was no significant relationship between the DRPs that occurred in the use of antibiotics in pediatric pneumonia patients and the patient's therapeutic

outcome (temperature and respiratory rate) where the p-value was p > 0.05. The study was conducted retrospectively by looking at the incidence of PCNE classification DRPs.

CONCLUSION

Evaluation of antibiotics prescribing appropriateness based on the PCNE method shows that 21.5% (11 regimens) of empiric antibiotics were appropriate and 78.8% (41 regimens) were inappropriate. The results of statistical tests show that there is a correlation of antibiotic prescriptions appropriateness and clinical response in terms of leukocyte count. However, the clinical response in terms of temperature and respiratory rate shows no significant correlation (p > 0.05).

ACKNOWLEDGEMENT

The authors would really like to explicit his gratitude to *Ristekbrin* (Minister of Research and Technology) for investment this research. Also, the health center director has accredited researchers to behavior this research. Lastly, the authors additionally would really like to expose gratitude to the manager who has guided in finishing this research.

DAFTAR PUSTAKA

Abunahlah, N., Elawaisi, A., Velibeyoglu, F. M., & Sancar, M. (2018). Drug related problems identified by clinical pharmacist at the Internal Medicine Ward in Turkey. *International Journal of Clinical Pharmacy*, *40*(2), 360–367. https://doi.org/10.1007/s11096-017-0585-5

Arnold, F. W., Wiemken, T. L., Peyrani, P., Ramirez, J. A., & Brock, G. N. (2013). Mortality differences among hospitalized patients with community-acquired pneumonia in three world regions: Results from the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study. *Respiratory Medicine*, *107*(7), 1101–1111. https://doi.org/10.1016/j.rmed.2013.04.003

Aulia, N. R. (2017). Analisa kuantitatif dengan metode atc/ddd dan penilaian drug related problem's penggunaan antibiotik di ruang isolasi rumah sakit umum daerah Cengkareng periode Januari-Desember 2016. *UIN Syarif Hidayatullah Jakarta*.

Blot, M., Croisier, D., Péchinot, A., Vagner, A., Putot, A., Fillion, A., Baudouin, N., Quenot, J.-P., Charles, P.-E., Bonniaud, P., Chavanet, P., & Piroth, L. (2014). A leukocyte score to improve clinical outcome predictions in bacteremic pneumococcal pneumonia in adults. *Open Forum Infect Dis*, *2*(1), 1–10. https://doi.org/10.1093/ofid/ofu075

Campanelli, C. M., Fick, D. M., Semla, T., & Beizer, J. (2012). Potentially inappropriate medication use in older adults: the American geriatrics society 2012 beers criteria. *Journal of the American Geriatrics Society*, *60*(4), 616–631. https://doi.org/10.1111/j.1532-5415.2012.03923.x

Dahesihdewi, A., Sugianli, A. K., & Parwati, I. (2019). The surveillance of antibiotics resistance in Indonesia: a current reports. *Bali Medical Journal*, *8*(2), 565. https://doi.org/10.15562/bmj.v8i2.1386

Faisal, F., Burhan, E., Aniwidyaningsih, W., Kekalih, A., Kedokteran, F., Indonesia, U., Ilmu, D., Komunitas, K., Kedokteran, F., & Indonesia, U. (2014). Penilaian respons pengobatan empiris pada pasien rawat inap dengan pneumonia komunitas evaluation of empirical treatment responsse in hospitalized patient Community Acquired Pneumonia. *Journal Respirologi Indonesia*, *34*(2), 60–70.

Farida, H., Gasem, M. H., Suryanto, A., Keuter, M., Zulkarnain, N., Satoto, B., van der Eijk, A. A., Djokomoeljanto, R., Wahyono, H., Verbrugh, H. A., Severin, J. A., & van den Broek, P. J. (2015). Viruses and Gram-negative bacilli dominate the etiology of community-acquired pneumonia in Indonesia, a cohort study. *International Journal of Infectious Diseases*, *38*, 101–107. https://doi.org/10.1016/j.ijid.2015.07.023

Firmansyah, M. A., Amin, Z., Loho, T., & Shatri, H. (2015). Faktor-faktor prediktor mortalitas community-acquired pneumonia dalam perawatan inap di rumah sakit Cipto Mangunkusumo, Jakarta. *Indonesian Journal of Chest Critical and Emergency Medicine*, *2*(2), 45–53.

Islam, Zainul, Qodariyah, S. M., & Nursehah, E. (2017). Penggunaan antibiotik pada terapi Community Acquired Pneumonia di RSUD pasar Rebo dan RSUD Tarakan di Jakarta tahun 2014. *Jurnal Sains Dan Teknologi Farmasi*, *19*(01), 1–8. https://doi.org/0.4103/0973-1482.148700

Istita, D. G., Laksmitawati, D. R., & Niken, M. (2020). Evaluasi penggunaan obat dan identifikasi drug related problem (DRP) pada pasien pneumonia di ruang rawat inap rumah sakit umum pusat Fatmawati Jakarta (periode Desember 2014 – Februari 2015). *Holistik Jurnal Kesehatan*, *14*(1), 129–139. https://doi.org/10.33024/hjk.v14i1.2391

Jenkins, T. C., Sakai, J., Knepper, B. C., Swartwood, C. J., Haukoos, J. S., Long, J. A., Price, C. S., & Burman, W. J. (2012). Risk factors for drug-resistant Streptococcus pneumoniae and antibiotic prescribing practices in outpatient community-acquired pneumonia. *Academic Emergency Medicine*, *19*(6), 703–706. https://doi.org/10.1111/j.1553-2712.2012.01365.x

Kemenkes. (2015). *Program pengendalian resistensi antimikroba di rumah sakit*. 1–31.

Kemenkes RI. (2011). Pedoman Umum Penggunaan Antibiotik. *Pedoman Umum Penggunaan Antibiotik*, *874*, 4. https://doi.org/10.1111/j.1524-4725.2011.01938.x

Kemenkes RI. (2019). *Profil Kesehatan Indonesia 2018 [Indonesia Health Profile 2018]*. http://www.depkes.go.id/resources/download/pusdatin/profil-kesehatan-indonesia/Data-dan-Informasi_Profil-Kesehatan-Indonesia-2018.pdf

Klompas, M., Ochoa, A., Ji, W., McKenna, C., Clark, R., Shenoy, E. S., Hooper, D., & Rhee, C. (2020). Prevalence of clinical signs within reference ranges among hospitalized patients prescribed antibiotics for Pneumonia. *JAMA Network Open*, *3*(7), 1–12. https://doi.org/10.1001/jamanetworkopen.2020.10700

Leyenaar, J. K., Shieh, M.-S., Lagu, T., Pekow, P. S., & Lindenauer, P. K. (2014). Comparative effectiveness of ceftriaxone in combination with a macrolide compared with ceftriaxone alone for pediatric patients hospitalized with Community Acquired Pneumonia. *Pediatr Infect Dis J*, *33*(4), 387–392. https://doi.org/10.1097/INF.0000000000000119

Li, Q., Jun, H., Dan, Q., Ming, L., Yeh, K., Sun, S., Li, L., & Liao, Y. (2019). Drug - related problems among hospitalized patients with COPD in mainland China. *International Journal of Clinical Pharmacy*, *41*(6), 1507–1515. https://doi.org/10.1007/s11096-019-00913-4

Mandell, L. A., Wunderink, R. G., Anzueto, A., Bartlett, J. G., Campbell, G. D., Dean, N. C., Dowell, S. F., File, T. M., Musher, D. M., Niederman, M. S., Torres, A., & Whitney, C. G. (2007). Infectious diseases society of america/american thoracic society consensus guidelines on the management of Community-Acquired Pneumonia in adults. *Clinical Infectious Diseases*, *44*(2), S27–S72. https://doi.org/10.1086/511159

Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., Cooley, L. A., Dean, N. C., Fine, M. J., Flanders, S. A., Griffin, M. R., Metersky, M. L., Musher, D. M., Restrepo, M. I., & Whitney, C. G. (2019). Diagnosis and treatment of adults with community-acquired pneumonia. *American Journal of Respiratory and Critical Care Medicine*, *200*(7), E45–E67. https://doi.org/10.1164/rccm.201908-1581ST

Mil, J. W. F. van, Horvat, N., & Westerlund, T. (2017). Classification for Drug related problems © 2003-2017. *'The PCNE Classification ,' V 8.01*, 1–10.

Mulyana, R. (2019). Terapi antibiotika pada Pneumonia usia lanjut. *Jurnal Kesehatan Andalas*, *8*(1), 172–177. https://doi.org/10.25077/jka.v8i1.987

Nie, X. M., Li, Y. S., Yang, Z. W., Wang, H., Jin, S. Y., Jiao, Y., Metersky, M. L., & Huang, Y. (2018). Initial empiric antibiotic therapy for community-acquired pneumonia in Chinese hospitals. *Clinical Microbiology and Infection*, *24*(6), 658.e1-658.e6. https://doi.org/10.1016/j.cmi.2017.09.014

Nuryah, A., Yuniarti, N., & Puspitasari, I. (2019). Prevalensi dan evaluasi kesesuaian penggunaan antibiotik pada pasien dengan infeksi methicillin resistant Staphylococcus Aureus di RSUP Dr. Soeradji Tirtonegoro Klaten. *Majalah Farmaseutik*, *15*(2), 123.

https://doi.org/10.22146/farmaseutik.v15i2.47911

PDPI. (2014). *Pneumonia komunitas* pedoman diagnosis & penatalaksanaan di Indonesia (2nd ed.). Badan Penerbit FKUI.

Permenkes RI. (2015). Tentang penyelenggaraan pelayanan kesehatan lanjut usia di pusat kesehatan masyarakat. *Kementrian Kesehatan Indonesia*, 1–140. https://doi.org/10.1017/CBO9781107415324.004

Pramudya, I. A. (2020). *Identifikasi drug related problem penggunaan antibiotik pada penyakit Pneumonia pasien anak di bangsal rawat inap rumah sakit Akademik Universitas Gadjah Mada*. Universitas Gajah Mada.

Presley, B., Setiabudi, I., Lestiono, L., & Ediyono, E. (2015). The influence of pharmaceutical care intervention on inpatient community acquired Pneumonia: A small randomized single blind study. *Jurnal Sains Farmasi & Klinis*, *2*(1), 84–90. https://doi.org/10.29208/jsfk.2015.2.1.54

Ramirez, J. A., Wiemken, T. L., Peyrani, P., Arnold, F. W., Kelley, R., Mattingly, W. A., Nakamatsu, R., Pena, S., Guinn, B. E., Furmanek, S. P., Persaud, A. K., Raghuram, A., Fernandez, F., Beavin, L., Bosson, R., Fernandez-Botran, R., Cavallazzi, R., Bordon, J., Valdivieso, C., … Carrico, R. M. (2017). Adults Hospitalized with Pneumonia in the United States: Incidence, Epidemiology, and Mortality. *Clinical Infectious Diseases*, *65*(11), 1806–1812. https://doi.org/10.1093/cid/cix647

Riskesdas, K. (2018). Hasil utama riset kesehata dasar (RISKESDAS). *Journal of Physics A: Mathematical and Theoretical*, *44*(8), 1–200. https://doi.org/10.1088/1751-8113/44/8/085201

Sari, E. F., Rumende, C. M., & Harimurti, K. (2017). Faktor–faktor yang berhubungan dengan diagnosis Pneumonia pada pasien usia lanjut. *Jurnal Penyakit Dalam Indonesia*, *3*(4), 183. https://doi.org/10.7454/jpdi.v3i4.51

Sari, I. P., Nuryastuti, T., Asdie, R. H., Pratama, A., & Estriningsih, E. (2017). Perbandingan pola terapi antibiotik pada Community- Acquired Pneumonia (CAP) di Rumah Sakit Tipe A dan B. *Jurnal Manajemen Dan Pelayanan Farmasi*, *7*(4), 168–174.

Sneha, K., Gayatri, M. S., Vinay, K., Prasad, A. R., & Sai, Y. S. (2019). A prospective study on assessment of rationality in prescribing antimicrobial agents at a tertiary care hospital. *Journal of Clinical and Diagnostic Research*, *August 2017*, 11–14. https://doi.org/10.7860/jcdr/2019/36921.12941

Sudibyo, J. (2019). Ajian praktek penggantian antibiotika terapi intravena ke oral pada pasien pneumonia di rawat inap RS PKU Muhammadiyah Gamping. *Journal of Petrology*. https://doi.org/10.1017/CBO9781107415324.004

WHO. (2014). *Antimicrobial Resistance*. *30*(4), 619–635. https://doi.org/10.1016/j.giec.2020.06.004

WHO. (2018). *Top 10 Causes of death*. https://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death.

Yulia, R., Mariza, J. W., Soedarsono, & Herawati, F. (2020). Bacterial profile and antibiotic use in Pneumonia patients At Dr. Soetomo General Hospital. *Current Respiratory Medicine Reviews*, *16*, 1–7. https://doi.org/10.2174/1573398x16666200217122825