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Rationality Analysis of Antibiotics for Community-Acquired Pneumonia in Adult Inpatients at X Hospital Sukoharjo

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Abstract

Community-acquired pneumonia in adult patients contributes to high morbidity and mortality rates. The rationality of antibiotics for community-acquired pneumonia pharmacotherapy can determine the result of patient clinical outcomes. The aim of this study was to determine antibiotic rationality for community-acquired pneumonia in adult inpatients at X Hospital Sukoharjo and the relationship between antibiotic rationality and its clinical outcomes. This study was an analytical cohort design with retrospective data in the form of patient medical records for the period 2022. The sampling method was carried out using total sampling with inclusion criteria being patients aged ≥ 18 years, male or female, diagnosed with community-acquired pneumonia, and receiving antibiotic therapy. The total samples were 102 who met the inclusion criteria which 52% were female gender and predominantly aged ≥ 65. The rationality analysis using the Gyssens method showed that 29.51% of antibiotics were given rationally with the highest number of irrationalities due to another more effective antibiotics (category IVA) at 54.90%. There was no significant relationship between antibiotic rationality and its clinical outcomes.

Keywords: Rationality, Antibiotic, Community-Acquired Pneumonia, Adult, Inpatient

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Introduction

Community-acquired pneumonia is one of the most causes of high morbidity and mortality in immunocompetent and immunocompromised patients[1]. The guidelines recommend that empiric antibiotics for community-acquired pneumonia should evaluated critically and individually[2]. The rationality of drugs, according to the WHO definition, is that a drug is said to be rational if patients receive drugs according to clinical need, dosage, duration, and costs that are affordable for them[3]. Rationality analysis of antibiotics should be analyzed periodically because the level of rationality in prescribing antibiotics is different from time to time depending on many things, such as patterns of germ resistance to antibiotics and/or the development of new antibiotics.

A study was carried out in three hospitals in Jakarta for the period of September 2016 to November 2017 with the result that 25.2% of antibiotics given rationally, where irrationality was caused by giving antibiotics that were too short (category IIIB)[4]. A study conducted at a private hospital in Yogyakarta for the period of January to December 2019 found that appropriate antibiotic prescribing was only 13.5% (category 0), while irrationality prescribing caused by other cheaper antibiotics (63.5 %) and there were other antibiotics with narrower spectrum (23.1%)[5]. Research at RSUP Dr. Kariadi Semarang, for the sampling period January 2017 to July 2019, the percentage of rational antibiotic administration was 88.78%[6]. Study in Ir. Soekarno General Hospital Sukoharjo for the 2017 period obtained data that the rational use of antibiotics was 7.4 percent while irrationality being caused by another more effective (59.02%) and less toxic antibiotics (28.60%)[7].

Drug rationality studies are important studies in the field of clinical pharmacy that show the rationality of drug administration influences patient clinical outcomes. Clinical outcomes that are influenced include drug effectiveness, drug toxicity, and costs during hospital treatment. Furthermore, irrational administration of antibiotics has the potential to increase bacterial resistance, which can ultimately affect its effectiveness. The absence of a similar study at X Hospital Sukoharjo will have an impact on the development of health services at the hospital and/or other hospitals. A study on the rationality of antibiotics is urgent because of the increasing resistance of common bacteria to several antibiotics commonly prescribed by doctors. This will affect the quality of health services in hospitals in the future. Data on antibiotic resistance that changes over time makes it important to carry out continuous studies on the rationality of antibiotics. Many cases of irrational antibiotic administration are found based on past studies. This study aimed to evaluate the rationality of antibiotics for community-acquired pneumonia in adult inpatients at X Hospital Sukoharjo and the relationship between rationality and clinical outcomes.

Method

Data Collections

This study is an observational analytic with a cohort retrospective design. Data was obtained from patient medical records from January - December 2022 with total sampling method. The inclusion criteria of this study are male or female inpatients aged ≥ 18 years old, diagnosed with community-acquired pneumonia, prescribed with an antibiotics. The exclusion criteria of this study are patient with an infectious disease other than community-acquired pneumonia (including hospital-acquired pneumonia or ventilator-associated pneumonia), immunocompromised patient, and patient forced to go home. We obtained

a sample with a total of 102 inpatient medical records that met the inclusion criteria.

Data collected include patient data (gender, age, length of stay), patients` clinical data (allergies, laboratory examinations, vital signs) and antibiotic administration data (name, dose, frequency, duration, route). This study has received ethical exemption from Ethics Committee of Kusuma Husada Surakarta University, Number: 99/UKH.L.02/EC/IX/2021.

Data Analysis

Analysis of patient data (gender, age, length of stay) descriptively in table form with percentages (%). Antibiotic rationality was analyzed using the Gyssens method (8). The relationship between rationality and clinical outcomes was determined using the Chi-Square test.

The clinical improvement was temperature ≤ 37.5°C, heart rate ≤ 100 beats/minute, respiratory rate ≤ 24 beats/min, systolic blood pressure ≥ 90 mmHg, oxygen saturation ≥ 90%, the ability to receive oral food intake and conditions of normal mental status (9). The patient's condition was monitored for three days after antibiotic use. Patients are clinically improved if they meet at least three of the criteria.

Result and Discussion

Patient data characteristics are shown in Table 1. The gender category shows that there are more female (51%) than male patients (49%). However, it is not significantly different. This is the same as the results of one study, in which the prevalence of pneumonia in women is greater than men[10].

At the age between 18 - 65 years, the age susceptible to pneumonia is 46 - 55 years and 56 - 65 years with a percentage of both 15.69%. This is follows other study that ages over 46 years have a greater prevalence of pneumonia[11]. These results also follows the 2018 National Basic Health Research Report (Riset Kesehatan Dasar Nasional) which states that the prevalence of pneumonia among those aged 45 years and over has increased nationally[12].

Table 1 shows that the patient length of stay in hospital with treatment days between 3 and 7 days shows the highest percentage with 92.16% compared to more than seven days. This follows the studies where the average patient length of stay in hospital for community-acquired pneumonia is less than seven days[5,11].

The comorbidities (table 2) that were frequently encountered in community-acquired pneumonia inpatients were heart and blood vessel disorders (68 cases), hormonal and metabolic disorders (46 cases), and electrolyte disorders (43 cases). This was follows the results of study at one of the hospitals in Sukoharjo in the 2018 period[11].

The most common hormonal and metabolic disorders include diabetes mellitus. The most common electrolyte disorders are hypokalemia, hyponatremia and hypocalcemia. One study found that electrolyte disturbances, especially hyponatremia and hypokalemia, were more common in patients with community-acquired pneumonia compared to other types of pneumonia[13]. Several comorbidities can affect the results of antibiotic therapy, including decreased kidney function, decreased liver function, heart disease, diabetes, and lung disease. Decreased liver and kidney function can result in antibiotic toxicity. Patients with heart disease may require close monitoring of cardiac function. Patients with diabetes may require antibiotic dose adjustments to prevent

drug interactions. Patients with lung disease require a longer or more intensive duration of therapy to treat infections.

Antibiotic selection should consider the most likely pathogen, local microbiology, risk factors for the particular pathogen, severity of pneumonia, patient preference and potential allergy to the antibiotic, and evaluation of cost-effectiveness[2]. Table 3 describes the administration of first-line empirical antibiotics for adult inpatients with community-acquired pneumonia in the 2022 period.

The antibiotic given to most patients as monotherapy was levofloxacin (39.2%), ceftriaxone (28.4%) and azithromycin (18.6%). Combination antibiotics were ceftriaxone and levofloxacin (2.9%), azithromycin and levofloxacin (1.9%), and azithromycin and cefoperazone (0.9%). First-line empirical antibiotics were given in single form at 94.1% and in combination at 5.9%. Guideline recommends respiratory fluoroquinolones or beta-lactam and macrolide as the standard empiric antibiotic regimen for hospitalized community-acquired pneumonia of mild/moderate severity without complications[1].

The first-line empirical antibiotic groups mostly given are fluoroquinolones. Cephalosporins were the second most prescribed empirical antibiotics. The third most common was azithromycin. A study regarding the relationship between giving azithromycin and mortality and cardiovascular events in pneumonia patients showed that there was a reduction in mortality rate and a slightly increase in the incidence of cardiovascular disorders in geriatric[14].

The effectiveness of monotherapy first-line empirical antibiotics with the three most prescribed antibiotics (levofloxacin, ceftriaxone and azithromycin), it was found that levofloxacin was the most effective among others. Levofloxacin is currently one of the mainstay antibiotic for community-acquired pneumonia besides a combination of beta-lactams and macrolides based on therapeutic guidelines[1,9] and with moderate severity[15]. The 2009 BTS guidelines for adult patients with moderate severity community-acquired pneumonia can be given azithromycin monotherapy[15] where the effectiveness of azithromycin monotherapy is also good (84.2%). Ceftriaxone monotherapy has the third percentage of effectiveness (75.9%) after levofloxacin and azithromycin. Intravenous ceftriaxone monotherapy can be the choice of empiric antibiotics in cases of community-acquired pneumonia without the risk of Pseudomonas aeruginosa infection in ICU patients based on the 2021 Indonesian Antibiotic Use Guidelines[16].

Table 4 shows data on second-line empiric antibiotics. Second-line antibiotics are all given empirically, step up from the first-line. Second-line antibiotics are most often given alone rather than in combination. All of the second-line antibiotics were effective for the patients. The most common antibiotic group are cephalosporins. The second most common group is macrolides. New macrolides (azithromycin, clarithromycin, roxithromycin) are antibiotics that can be added if an atypical bacterial infection is suspected. Besides new macrolides, other alternatives include adding respiratory fluoroquinolones such as levofloxacin[9].

There were no patients who received definitive antibiotics in the medical records taken. All patients who are ineffective with first-line antibiotics can experience improvement/cure when given second-line antibiotics.

Rationality analysis of the antibiotic using the Gyssens method in Table 5 shows that from

102 samples, only 30 samples were found in category 0 (rational) (29.41%). As many as 70.59% (72 samples) fall into the irrational category (categories I – VI). Another study in a hospital in Malang from January 2017 to June 2019 showed that rational antibiotics were 13.24%[17]. Rationality analysis of antibiotics in a private hospital in Yogyakarta from January – December 2019 showed that rational antibiotic were 13.5%[5]. A study on the rationality of empirical antibiotics for pneumonia at the Kariadi Hospital from January 2017 to May 2019 showed that rational antibiotics were 88.78%[6]. A study on the rationality of antibiotics for severe pneumonia in children at a health center in southwestern Uganda reported that rational antibiotic prescribing was 24.9%, of which 75.1% was considered irrational[18].

Differences in levels of rationality may be caused by internal, external, and economic factors. Internal factors can include the availability of resources, the quality of human resources, hospital policies, and procedures. External factors can include government regulations and policies, availability of antibiotics, and pressure from patients and families. Economic factors include the cost of antibiotics and patient care costs.

The guidelines used are the PDPI CAP Guidelines 2nd Edition, the 2017 Clinical Practice Guidelines for Doctors in Primary Care Facilities, the 2019 CAP Adults ATS/ IDSA Guidelines and the 2021 Antibiotic Use Guidelines (PPAB) of the Indonesian Ministry of Health to assess the rationality of antibiotic selection. All analyses use the Gyssens method.

The administration of monotherapy ceftriaxone or azithromycin falls into category IVA, based on literature the recommended antibiotics are levofloxacin monotherapy or a combination of beta-lactams and macrolides. Besides, monotherapy preparations of ciprofloxacin, gentamicin, meropenem and azithromycin are included in category IVA[1,9,16,19]. The use of ceftriaxone and azithromycin monotherapy is possible because these antibiotics have been able to produce successful therapy. So, hospital doctors should consider using these antibiotics.

Antibiotics with a duration that is too long are azithromycin, which has a duration based on the literature of 3 days. Apart from that, the duration of the antibiotic levofloxacin based on the literature is 3-5 days[16]. Using antibiotics that are too long in duration is not recommended because bacteria have a greater chance of becoming resistant[20]. Doctors prescribe antibiotics for a longer duration because they consider that the therapeutic effect has not been achieved. So the doctor extends the duration of treatment.

The use of antibiotics that were too short in duration was found in ceftriaxone, levofloxacin and azithromycin antibiotics. The recommended antibiotic duration for ceftriaxone and levofloxacin is 3 – 5 days and 3 days for azithromycin[16]. Duration of antibiotics for too short can not achieve maximum treatment results[21]. The use of levofloxacin in patients with kidney disorders should also require a dose adjustment from the usual dose of 750 mg/24 hours. Antibiotics such as ceftriaxone are safer for patients with kidney disorders[16,22]. Doctors prescribe antibiotics for a shorter duration because they consider the therapeutic effect that has been achieved or the patient's clinical outcome has improved. And also by considering economic factors regarding patient care costs.

Incorrect dosage occurred at ceftriaxone 2 grams + levofloxacin 750 mg/24 hours, whereas according to literature, ceftriaxone

1 gram + levofloxacin 750 mg/24 hours. Another incorrect dosage was found in levofloxacin monotherapy 500 mg/24 hours, whereas according to the literature, 750 mg/24 hours was given. Furthermore, azithromycin monotherapy 250 mg/24 hours whereas incorrect according to the literature, 500 mg/24 hours[16,19]. Inappropriate intervals are based on the patient's medical record data of administration of antibiotics is not steady as the patient does not receive antibiotics at the proper administration schedule. Incorrect route of administration occurs in the oral administration of azithromycin, whereas in the literature, inpatients are advised to take the intravenous route[16]. Giving antibiotic doses that do not comply with guidelines is possible because doctors do not follow existing treatment guidelines.

Table 6 shows the relationship between rationality and clinical outcomes. A p-value was obtained of 0.763, which means there is no significant relationship between the rationality of antibiotics and its clinical outcomes (p-value > 0.05). This means that the rationality of antibiotics does not affect the clinical outcomes . This is the same as previous studies[4-6]. Even though the irrational use of drugs does not have much influence on the effectiveness of drug therapy in this study, it can cause an increase in antibiotic resistance, morbidity, mortality, and treatment costs[23]. This ultimately becomes a national health burden that influences national health costs.

The rationality of antibiotic use can be improved by some steps such as establishing antimicrobial stewardship programs in hospitals more effective, as well as implementing a restrictive infectious control system[23,24]. This study has several limitations, including limited the number of samples taken, and not taking data on toxicity and costs in terms of their impact on the rationality of treatment.

Conclusion

This study concluded that 29.41% were in the rational category, while 70.59% were in the irrational category. Irrationality is caused by another more effective antibiotics (category IVA) at 54.90%, use of antibiotics that are too long (category IIIA) at 14.71%, use of antibiotics that are too short (category IIIB) at 12.75%, other safer antibiotics (category IVB) at 9.80%, inappropriate doses (category IIA) at 8.82%, inappropriate administration intervals (category IIB) at 7.84% and inappropriate administration routes (category IIC) at 3.92%. There was no significant relationship between antibiotic rationality and its clinical outcomes.

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Conflict of Interest

None declared.

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Table 1. Patient Data Characteristics.

Patient Data	Total (n=102)	Percentage (%)
Sex		
Male	50	49
Female	52	51
Age (Year)		
18-25	12	11.76
26-35	5	4.90
36-45	15	14.71
46-55	16	15.69
56-65	16	15.69
>65	38	37.25
Length of Stay (days)		
3 – 7	94	92.16
> 7	8	7.84

Table 2. Comorbidities.

Comorbidities	Total	Percentage (%)
cardiovascular	68	24.4
metabolic and hormonal	46	16.5
electrolyte	43	15.4
renal	29	10.4
hematology	25	8.9
respiratory	24	8.6
gastrointestinal	19	6.8
neurology	8	2.9
bone and joint	6	2.1
tumour	4	1.4
urology	2	0.7
liver	2	0.7
psychiatry	1	0.3
nutrition	1	0.3

Note : 1 patient can have more than one comorbidity

Table 3. First-line Antibiotics Used.

Descriptions	Total (%)	Effectivity (%)
Antibiotic Name		
Monotherapy		
Levofloxacin	40 (39.2%)	36 (90.0%)
Ceftriaxone	29 (28.4%)	22 (75.9%)
Azithromycin	19 (18.6%)	16 (84.2%)
Ciprofloxacin	4 (3.9%)	4 (100%)
Meropenem	2 (1.9%)	2 (100%)
Cefotaxime	1 (0.9%)	1 (100%)
Gentamicin	1 (0.9%)	0 (0%)
Combinations		
Ceftriaxone + Levofloxacin	3 (2.9%)	3 (100%)
Azithromycin + Levofloxacin	2 (1.9%)	2 (100%)
Azithromycin + Cefoperazone	1 (0.9%)	1 (100%)
Antibiotic Regimen		
Monotherapy	96 (94.1%)	81 (84.4%)
Combination	6 (5.9%)	6 (100%)
Antibiotic Group		
Fluoroquinolone	49	
Cephalosporine	34	
Macrolide	22	
Carbapenem	2	
Aminoglycosides	1	

Table 4. Second-line Antibiotics Used.

Descriptions	Total
Antibiotic Name	
Azithromycin	5
Levofloxacin	3
Ceftriaxone	2
Ceftazidime	1
Metronidazole	1
Ampicillin-Sulbactam	1
Levofloxacin + Ceftazidime + Cefotaxime	1
Ceftazidime + Gentamicin + Cefixime	1
Antibiotic Regimen	
Monotherapy	12
Combination	3
Antibiotic Group	
Beta-lactams	7
Macrolide	5
Fluoroquinolone	4
Aminoglycosides	1
Nitroimidazole	1

Table 5. Rationality Analysis of Antibiotics Given Using Gyssens Method.

Category	Total (n = 102) (%)
Rational	(29.41%)
Category 0 (rational)	30
Not Rational	(70.59%)
Category VI (data complete)	0
Category V (antibiotic not indicated)	0
Category IVA (others are more effective)	56
Category IVB (others are more safe)	10
Category IVC (others are more cheap)	0
Category IVD (others are more narrow spectrum)	0
Category IIIA (duration too long)	15
Category IIIB (duration too short)	13
Category IIA (incorrect dose)	9
Category IIB (incorrect interval)	8
Category IIC (incorrect rute)	4
Category I (incorrect time of administration)	0

Table 6. Relationship between rationality and clinical outcome.

	Rational	Not Rational	P-Value*	Odds ratio	95% CI
Improved	25 (83%)	60 (86%)	0.763	0.806	0.250-2.597
Not-yet improved	5 (17%)	10 (14%)			

* Fisher-Exact Test