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RESEARCH ARTICLE

RATIONALITY OF ANTIBIOTIC PRESCRIPTIONS AMONG OUTPATIENTS IN THE INTERNAL MEDICINE CLINIC AT PERSAHABATAN GENERAL HOSPITAL JULY–SEPTEMBER 2023

(*RASIONALITAS PERESEPAN ANTIBIOTIK PADA PASIEN RAWAT JALAN POLI PENYAKIT DALAM DI RSUP PERSAHABATAN PERIODE JULI–SEPTEMBER 2023)*

Astrid Nada Artanti[1], Ima Maria[2], Eldiza Puji Rahmi[1], Dhigna Luthfiyani Citra Pradana[1], Diliana[3]

[1]Pharmacy Study Program, Faculty of Medicine, UPN "Veteran" Jakarta, Indonesia
[2]Bachelor of Medicine Program, Faculty of Medicine, UPN "Veteran" Jakarta, Indonesia
[3]Persahabatan Hospital, Ministry of Health of the Republic of Indonesia

Correspondence Email: imamaria@upnvj.ac.id

ABSTRACT

Antibiotic use has increased in both developing countries, such as Indonesia, and developed countries, such as Japan and Australia. This trend may lead to a rise in antibiotic resistance if antibiotics are used irrationally. This study aimed to evaluate antibiotic prescribing patterns using the *Gyssens* method among adult outpatients in the Internal Medicine Clinic at Persahabatan General Hospital during the period of July–September 2023. This was a descriptive study with a *cross-sectional* design. Data were collected retrospectively from the medical records of adult outpatients attending the Internal Medicine Clinic during the study period. Of the 30 patient records that met the inclusion and exclusion criteria, the age group 51–60 years represented the largest proportion of antibiotic prescriptions (46.67%). Levofloxacin was the most frequently prescribed antibiotic (30.3%). Based on the Gyssens method, 88.8% of prescriptions were classified as rational, while 11.1% were irrational. In conclusion, 88.8% of antibiotics prescribed for adult outpatients in the Internal Medicine Clinic at Persahabatan General Hospital during July–September 2023 were deemed rational according to the *Gyssens* method.

Keywords : antibiotics, *gyssens* method, outpatient

ABSTRAK

Penggunaan antibiotik telah mengalami peningkatan baik di negara berkembang, seperti Indonesia, maupun di negara maju, seperti di Jepang dan Australia. Hal ini berpotensi meningkatkan kasus resistensi terhadap antibiotik apabila penggunaan antibiotik tidak rasional. Penelitian ini bertujuan untuk mengevaluasi peresepan antibiotik dengan metode Gyssens pada pasien dewasa rawat jalan poli penyakit dalam di RSUP Persahabatan periode Juli–September 2023. Penelitian ini merupakan studi deskriptif dengan desain studi potong lintang (cross-sectional). Pengumpulan data bersifat retrospektif dari rekam medis pasien

dewasa rawat jalan poli penyakit dalam di RSUP Persahabatan periode Juli−September 2023. Dari 30 rekam medis pasien yang telah memenuhi kriteria inklusi dan eksklusi, menunjukkan bahwa kelompok usia 51-60 tahun merupakan kelompok usia yang paling banyak menerima peresepan antibiotik (46,67%), Levofloksasin merupakan jenis antibiotik yang paling banyak diresepkan (30,3%), 88,8% peresepan antibiotik secara rasional, dan 11,1% peresepan antibiotik tidak rasional. Dapat disimpulkan bahwa sebesar 88,8% antibiotik yang diresepkan pada pasien dewasa rawat jalan poli penyakit dalam di RSUP Persahabatan periode Juli−September 2023 sudah diberikan secara rasional berdasarkan metode Gyssens.

Kata Kunci: antibiotik, metode gyssens, rawat jalan

INTRODUCTION

Antibiotics are drugs used to treat bacterial infections.[1] However, their use has continued to increase significantly to date. A study conducted in Japan between 2013 and 2018 reported an increase in macrolide antibiotic prescriptions from 958,028 to 1,939,474.[2] Research conducted in Australia between March and May 2023 found that the most frequently prescribed antibiotic for hospitalized patients was amoxicillin–clavulanic acid (28%).[3]

Antibiotics also play a significant role in combating diseases, particularly in developing countries where infectious diseases remain a major challenge. A study in Malaysia showed that only 128 out of 338 antibiotic prescriptions complied with the guidelines of the Malaysian Ministry of Health.[4] In Indonesia, a study among adult patients in the intensive care unit (ICU) of Konawe Hospital, Southeast Sulawesi, found that 81.1% of antibiotic prescriptions were irrational.[5] Similarly, research conducted at Kanjuruhan District Hospital, Malang, reported that 80% of antibiotic prescriptions were irrational.[6] Another study at Tora Belo Hospital, Palu, which assessed drug use based on prescribing and patient-care indicators according to WHO standards, found that 45.52% of antibiotic prescriptions were non-compliant with WHO standards, which should be ≤30%.[7] Irrational antibiotic use in several hospitals in Indonesia poses a serious risk of increasing bacterial resistance. It is estimated that antibiotic resistance directly contributed to 1.27 million global deaths in 2019.[8] Therefore, evaluating antibiotic use is crucial to prevent the emergence of antibiotic resistance.

The quality of antibiotic use can be assessed using the Gyssens method, which is commonly employed to evaluate the appropriateness of antibiotic use, particularly in Indonesia. However, its application remains mostly limited to hospitalized patients. This study aims to evaluate antibiotic prescribing patterns

using the Gyssens method among adult outpatients in the Internal Medicine Clinic during the period of July–September 2023 at Persahabatan General Hospital.

METHODS

This study employed a cross-sectional design with retrospective data collection from the medical records of adult outpatients attending the Internal Medicine Clinic at Persahabatan General Hospital, East Jakarta, during the period of July–September 2023. Data collection began in March 2024 and was obtained from the Medical Records Department of Persahabatan General Hospital.

The inclusion criteria were outpatients aged 18–60 years who received antibiotic therapy during the period of July–September 2023 in the Internal Medicine Clinic, were registered under the National Health Insurance (BPJS), and had complete data on age, sex, diagnosis, and antibiotic prescription, including drug name, dosage, and frequency of administration. The exclusion criterion was incomplete medical record data.

The sample size was calculated using the Lemeshow formula, as follows:

$$n = \left(\frac{\left(Z_{\frac{1-\alpha}{2}} \sqrt{P_1(1-P_1)} + Z_{1-\beta} \sqrt{P_2\,(1-P_2)} \right)^2}{(P_2 - P_1)^2} \right)$$

Description :

n : minimum required sample size
α : level of significance (0.05)
$\frac{Z_{1-\alpha}}{2}$: Z-value corresponding to α for a two-sided test (1.96)
$Z_{1-\alpha}$: Z-value corresponding to a 95% confidence level
1-β : power of test (90%)
$Z_{1-\beta}$: Z-value for 90% test power (1.28)
P1 : proportion of rational antibiotic use at Gatot Soebroto Army Hospital (0.738).[9]
P2 : proportion of rational antibiotic use at Persahabatan General Hospital (0.417)[10]

Based on the calculation using the Lemeshow formula, the minimum required sample size was 22 samples, which was then increased by 10% to account for potential data loss, resulting in a minimum of 25 samples. In this study, a total of 472 medical records of adult outpatients from the Internal Medicine Clinic during the period of July–September 2023 were reviewed. After individual screening, 30 medical records met the inclusion and exclusion criteria and were included in the analysis.

The Gyssens algorithm evaluates antibiotic use based on the following appropriateness: indication; availability of more effective, safer, or more cost-effective alternatives; the spectrum of antimicrobial activity; and the suitability of duration, dosage, route, and timing of administration.[11] The assessment flow using the Gyssens method is illustrated in Figure 1.

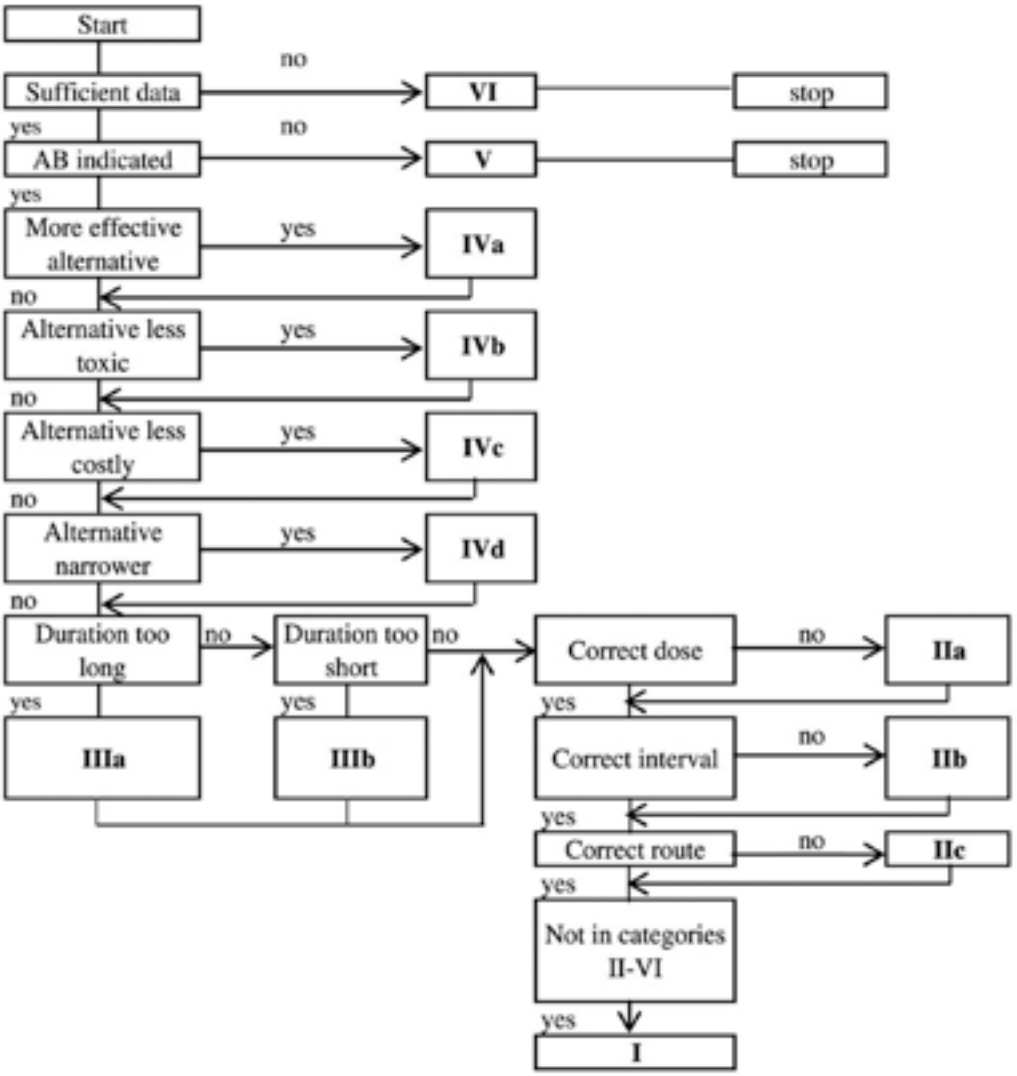

Figure 1 Flowchart of antibiotic prescription evaluation using the *Gyssens* Method Adapted from: Regulation of the Minister of Health of the Republic of Indonesia No. 8 of 2015 on the Hospital Antimicrobial Resistance Control Program.

This study received ethical approval from the Research Ethics Committee of Universitas Pembangunan Nasional "Veteran" Jakarta (No. 87/III/2024/KEP) and the Health Research Ethics Committee of Persahabatan General Hospital (No. 0082/KEPK-RSUPP/04/2024).

RESULTS AND DISCUSSION

The largest age group in this study was 51–60 years. Similar findings were reported in a study of hospitalized patients at the Department of Internal Medicine, Diponegoro National Hospital, where the majority of patients were aged 46–65 years

(50%).[12] This may be attributed to age-related changes in immunity and physiological function, such as decreased neutrophil bactericidal activity, reduced macrophage phagocytic capacity, and increased levels of proinflammatory cytokines.[13] Click or tap here to enter text.

Table 1 Characteristics of adult outpatients prescribed antibiotics in the internal medicine clinic at Persahabatan General Hospital, July–September 2023

Category	Frequency (n=30)	Percentage (%)
Sex		
Male	16	53
Female	14	47
Age (years)		
18-20	0	0
21-30	3	10
31-40	5	16.67
41-50	8	26.67
51-60	14	46.67

Source: Secondary data from the Medical Records Department of Persahabatan General Hospital, July–September 2023.

In this study, the majority of patients were male. This finding is consistent with previous study conducted among referral patients who had received antibiotic therapy in the inpatient ward of RSPAL Dr. Ramelan Hospital, Surabaya, which reported that most subjects were male, accounting for 24 individuals (55.82%).[14]

Table 2 Distribution of infectious disease diagnoses by age group among adult outpatients prescribed antibiotics in the internal medicine clinic at Persahabatan General Hospital, July–September 2023

Diagnosis	Age (years)					Frequency (n=30)	Percentage (%)
	18-20	21-30	31-40	41-50	51-60		
Gluteal abscess	0	1	0	0	0	1	3.33
Anal fistula	0	0	1	0	0	1	3.33
Acute gastroenteritis	0	0	0	2	2	4	13.33
HIV infection	0	1	0	1	0	2	6.67
HIV with pulmonary tuberculosis	0	0	3	1	1	5	16.67
Urinary tract infection	0	0	1	0	1	2	6.67
Acute respiratory infection (ARI)	0	0	0	1	1	2	6.67
ARI with toxoplasmic encephalitis	0	1	0	0	0	1	3.33
Ulcerative colitis	0	0	0	0	4	4	13.33
Pneumonia	0	0	0	1	1	2	6.67
Postoperative cholecystectomy	0	0	0	1	0	1	3.33
Postoperative lymphadenectomy	0	0	0	0	1	1	3.33
Liver cirrhosis with ascites	0	0	0	0	1	1	3.33
Pulmonary tuberculosis	0	0	0	0	2	2	6.67
Diabetic ulcer	0	0	0	1	0	1	3.33

Source: Secondary data from the Medical Records Department of Persahabatan General Hospital, July–September 2023.

The most prevalent infectious disease diagnosis in this study was HIV with pulmonary tuberculosis (TB). Pulmonary TB is among the most common opportunistic infections affecting patients with HIV.[15] The increased risk of TB infection in HIV patients may result from a reduced CD4 cell count, functional impairment of TB-specific T cells, and a decreased macrophage ability to inhibit Mycobacterium tuberculosis activity.[16]

In this study, cotrimoxazole at a dosage of 960 mg once daily was prescribed for patients with HIV and pulmonary TB. This prescription is consistent with the HIV Management Guidelines issued by the Indonesian Ministry of Health (2019), which strongly recommend cotrimoxazole prophylaxis at a dose of 960 mg once daily for HIV-positive patients receiving anti-tuberculosis therapy.[17]

Table 3 Profile of antibiotic use based on infectious disease diagnoses among adult outpatients prescribed antibiotics in the internal medicine clinic at Persahabatan General Hospital, July–September 2023

Type of Antibiotic	Number of Antibiotics f (%)	Infectious Disease Diagnosis		Supporting Examinations
Azithromycin	2	(4,44)	Acute respiratory infection (ARI)	Chest CT scan, hematology
	2	(4,44)	Pneumonia	Chest CT scan
	1	(2,22)	Pulmonary tuberculosis	Hematology, urinalysis
Ethambutol	3	(6,67)	Pulmonary tuberculosis	Hematology
Isoniazid	3	(6,67)	Pulmonary tuberculosis	Hematology
Clindamycin	1	(2,22)	Toxoplasma encephalitis	–
	1	(2,22)	Diabetic ulcer	Hematology
Cotrimoxazole	2	(4,44)	HIV	Hematology
	5	(11,11)	HIV + pulmonary tuberculosis	Hematology
Levofloxacin	1	(2,22)	Gluteal abscess	Hematology
	1	(2,22)	Anal fistula	Colonoscopy
	3	(6,67)	Acute gastroenteritis	–
	1	(2,22)	ARI	–
	1	(2,22)	Ulcerative colitis	Colonoscopy
	1	(2,22)	Post-lymphadenectomy	–
	1	(2,22)	Hepatic cirrhosis with ascites	Abdominal ultrasound, Fibroscan, hematology
	1	(2,22)	Pulmonary tuberculosis	Microbiological culture
Pyrazinamide	3	(6,67)	Pulmonary tuberculosis	Hematology
Rifampicin	3	(6,67)	Pulmonary tuberculosis	Hematology
Cefuroxime	1	(2,22)	Pneumonia	Chest CT scan
Ciprofloxacin	1	(2,22)	Acute gastroenteritis	Hematology
	2	(4,44)	Urinary tract infection	Microbiological culture
	2	(4,44)	Ulcerative colitis	Microbiological culture, colonoscopy
	1	(2,22)	Post-cholecystectomy	Laparoscopic cholecystectomy, hematology
Sulfasalazine	2	(4,44)	Ulcerative colitis	Colonoscopy
Total Antibiotics	**45**	**(100)**		

This study showed that levofloxacin was the most frequently prescribed antibiotic compared with other types. Similar findings were reported in both

private and tertiary hospitals in Bandung, West Java.[18],[19] This indicates that the high use of levofloxacin has been observed across several hospitals in Indonesia. The widespread use of levofloxacin may be attributed to its broad spectrum of activity against both Gram-positive and Gram-negative bacteria.

Table 4 frequency distribution of antibiotic evaluation results using the gyssens method among adult outpatients in the internal medicine clinic (Qualitative Assessment)

Gyssens Category		Number of Antibiotics	Percentage (%)
VI	Incomplete medical record data; evaluation not possible	0	0
V	No indication for antibiotic use	0	0
IVa	There is a more effective alternative antibiotic	5	11.1
IVb	There is a less toxic or safer alternative antibiotic	0	0
IVc	There is a less expensive alternative antibiotic	0	0
IVd	There is an alternative antibiotic with a narrower spectrum	0	0
IIIa	Duration of antibiotic therapy too long	0	0
IIIb	Duration of antibiotic therapy too short	0	0
IIa	Incorrect antibiotic dosage	0	0
IIb	Incorrect dosing interval	0	0
IIc	Incorrect route of administration	0	0
I	Incorrect timing of antibiotic administration	0	0
0	Appropriate and rational antibiotic use	40	88.8
Total		45	100

Among the antibiotics classified as category IVa, all five were levofloxacin. Of the five inappropriate levofloxacin prescriptions, three were for patients with acute gastroenteritis (AGE), one for a patient with hepatic cirrhosis and ascites, and one for a patient with ulcerative colitis. In patients with AGE presenting with diarrhea occurring 6–10 times per day and abdominal pain, levofloxacin prescription was inconsistent with the Infectious Diseases Society of America (IDSA) Guidelines, 2017, which recommend ciprofloxacin 500 mg every 12 hours for 3–5 days for diarrheal cases.[20] Ciprofloxacin has been shown to significantly reduce the duration of noninvasive diarrhea by 32.5% and increase the rate of complete recovery within 72 hours.[21] However, due to increasing resistance to fluoroquinolones, azithromycin 500 mg once daily for three days may serve as an alternative. In addition, no stool culture was performed, making the causative pathogen uncertain.

The prescription of levofloxacin 500 mg once daily for seven days in a patient with hepatic cirrhosis and ascites accompanied by right upper abdominal pain

was also deemed inappropriate. A more effective antibiotic is ciprofloxacin 500 mg once daily,[22] which is recommended as prophylaxis and should be continued until the ascitic condition improves.

Similarly, levofloxacin 500 mg once daily for seven days in a patient with ulcerative colitis was considered less appropriate than ciprofloxacin. Ciprofloxacin is more effective in managing gastrointestinal infections due to its superior tissue penetration and bioavailability. Based on its pharmacokinetic profile, ciprofloxacin allows better absorption and distribution in the intestinal mucosa compared with levofloxacin.[23] Ciprofloxacin also exhibits a broader spectrum of activity against Gram-negative bacteria, particularly Escherichia coli, Pseudomonas aeruginosa, and Campylobacter jejuni, which are commonly implicated in gastrointestinal infections.[24] Furthermore, ciprofloxacin may contribute to remission induction in ulcerative colitis when combined with standard anti-inflammatory therapy.[25] Although levofloxacin is effective against various pathogens, it is pharmacodynamically more suitable for treating respiratory tract infections[26] and urinary tract infections.[27]

In ulcerative colitis, damage to the colonic mucosal barrier triggers inflammation and ulceration.[28] Impairment of the immune system compromises the ability to eliminate pathogens such as *Campylobacter spp*., leading to inflammation and recurrent episodes of acute gastroenteritis.[29] *Campylobacter jejuni* infection can stimulate mucosal immune responses, exacerbating inflammation and complications.[30] In the pathogenesis of ulcerative colitis, ciprofloxacin inhibits DNA gyrase (topoisomerase II and IV), thereby preventing DNA replication and inducing strand breaks.[31] Its effectiveness against Gram-negative bacteria makes ciprofloxacin suitable for treating both ulcerative colitis and acute gastroenteritis.

In this study, 88.8% of antibiotic prescriptions at Persahabatan General Hospital were rational, aligning with findings from a type A hospital in Jakarta, RSPAD Gatot Soebroto, which reported 73.8% rational prescriptions using the Gyssens method.[9] In contrast, studies at Diponegoro National Hospital and Kanjuruhan District Hospital, Malang, reported higher rates of irrational prescriptions.[6,12] These differences may be attributed to variations in hospital type and the extent of Gyssens method implementation for antibiotic use evaluation.

CONCLUSION

Based on the study findings, 88% of antibiotic prescriptions for adult outpatients

in the Internal Medicine Clinic at Persahabatan General Hospital during the period of July–September 2023 were classified as rational. However, more comprehensive microbiological culture data are required to support the provision of truly rational antibiotic therapy.

CONFLICT OF INTEREST

The authors declare no conflict of interest in this study.

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