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Evaluation of antibiotic use rationality in typhoid fever patients at TK IV 02.07.04 Hospital, Bandar Lampung, using the Gyssens method

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ABSTRACT
Typhoid fever, an infection caused by *Salmonella typhi*, remains an endemic public health problem in Indonesia, with an estimated 11–20 million cases reported globally each year. Antibiotics are the mainstay of treatment; however, irrational use may lead to bacterial resistance and increased complications. This study aimed to evaluate the rationality of antibiotic use in patients with typhoid fever at TK IV 02.07.04 Hospital, Bandar Lampung, in 2023 using the Gyssens method. An analytical observational study with a cross-sectional design was conducted using 121 medical records of typhoid fever patients from 2023, selected through purposive sampling based on predefined inclusion criteria. Data were analyzed descriptively using the Gyssens method to classify the rationality of antibiotic use (categories 0–VI) and processed using Microsoft Excel. The majority of patients were male (71%), aged 20–35 years (83%), and had a body weight of 61–90 kg (69%). Ceftriaxone was administered to all patients (100%), predominantly at a dose of 1 gram every 12 hours (98%) and for a duration of 5–6 days (76%). Gyssens evaluation revealed that 75% of antibiotic use was classified as rational (category 0), while 25% was irrational, mainly due to excessively short duration of therapy (24%, category IIIB) and inappropriate dosing (1%, category IIA). The use of ceftriaxone was generally consistent with the Indonesian Ministry of Health Regulation No. 28 of 2021; however, deviations related to treatment duration of less than five days and suboptimal dosing frequency contributed to irrational use. Male patients exhibited a higher risk, potentially associated with increased outdoor activities and lower hygiene practices. These findings highlight the need for stricter monitoring to minimize antimicrobial resistance and optimize therapeutic outcomes. In conclusion, most antibiotic use in typhoid fever patients was rational (75%); nevertheless, a substantial proportion (25%) remained irrational due to noncompliance with recommended duration and dosing. Enhanced adherence to national guidelines and improved hygiene education are recommended to support prevention efforts and control bacterial resistance.
Keyword: *antibiotic, ceftriaxone, gyssens, typhoid fever*

ABSTRAK
Demam tifoid, infeksi akibat Salmonella typhi, merupakan masalah kesehatan endemik di Indonesia dengan estimasi 11-20 juta kasus global per tahun. Pengobatan primer melibatkan antibiotik, namun penggunaan irasional dapat menyebabkan resistansi bakteri dan komplikasi. Penelitian ini bertujuan mengevaluasi kerasionalan penggunaan antibiotik pada pasien demam tifoid di Rumah Sakit TK IV 02.07.04 Bandar Lampung tahun 2023 menggunakan metode Gyssens. Studi observasional analitik dengan desain cross-sectional ini menggunakan sampel 121 rekam medik pasien demam tifoid tahun 2023, dipilih melalui purposive sampling berdasarkan kriteria inklusi. Data dianalisis secara deskriptif dengan metode Gyssens untuk mengkategorikan kerasionalan antibiotik (kategori 0-VI), diolah menggunakan Microsoft Excel. Sebanyak 71% pasien laki-laki, 83% berusia 20-35 tahun, dan 69% berat badan 61-90 kg. Antibiotik seftriakson diberikan pada 100% pasien, dengan dosis 1 gram setiap 12 jam (98%) dan durasi 5-6 hari (76%). Evaluasi Gyssens menunjukkan 75% penggunaan

rasional (kategori 0), sementara 25% tidak rasional, termasuk 24% durasi terlalu singkat (kategori IIIB) dan 1% dosis tidak tepat (kategori IIA). Penggunaan seftriakson selaras dengan Pedoman PMK No. 28 Tahun 2021, tetapi penyimpangan pada durasi <5 hari dan frekuensi dosis rendah menimbulkan irasionalitas. Faktor risiko lebih tinggi pada laki-laki akibat aktivitas luar ruangan dan higiene rendah. Temuan ini menekankan perlunya pengawasan ketat untuk mengurangi resistansi dan optimalisasi terapi. Mayoritas penggunaan antibiotik pada pasien demam tifoid rasional (75%), tetapi 25% tidak rasional karena durasi dan dosis tidak sesuai pedoman. Rekomendasi termasuk peningkatan kepatuhan terhadap PMK No. 28 Tahun 2021 serta edukasi higiene untuk pencegahan dan pengendalian resistansi bakteri.
Keyword: *antibiotik, seftriakson, gyssens, demam tifoid,*

1. Introduction

Infectious diseases remain a major public health problem in Indonesia [1]. Typhoid fever, caused by the Gram-negative bacterium *Salmonella typhi*, is an infectious disease that affects the gastrointestinal tract and is endemic in Indonesia [2][3]. The disease is transmitted through contaminated food and water, as well as through direct contact, with hygiene practices playing a crucial role in its transmission [4]. Globally, an estimated 11–20 million people suffer from typhoid fever each year [5]. In Indonesia, typhoid fever ranks as the third most common cause of hospitalization in hospitals nationwide [3][6]. The primary treatment for typhoid fever is antibiotic therapy [6].

Irrational use of antibiotics may result in significant adverse consequences, including bacterial resistance, increased toxicity, and drug-related side effects [8]. Antimicrobial resistance often arises from inappropriate antibiotic prescribing, such as unclear indications, incorrect dosing or duration, and improper routes of administration. Therefore, the evaluation of antibiotic use has become a critical quality indicator within hospital-based antimicrobial resistance control programs [9]. The use of broad-spectrum antibiotics, particularly cephalosporins—commonly indicated for respiratory, urinary tract, and soft tissue infections—when prescribed for other indications, may further contribute to the development of resistance [12]. The Gyssens method is widely used to assess the appropriateness of antibiotic use by classifying prescriptions into rational and irrational categories.

Previous studies employing the Gyssens method have reported a substantial proportion of irrational antibiotic use. For instance, one study identified that 60% of antibiotic prescriptions were irrational [5], while another study reported that 10% of antibiotic use involved excessively prolonged duration [8]. In light of these concerns, this study is essential to evaluate the rationality of antibiotic use in patients with typhoid fever, with the aim of improving therapeutic effectiveness, preventing bacterial resistance, and enhancing the quality of healthcare services by ensuring appropriate drug selection and dosing tailored to patient conditions [7]. Therefore, this study aimed to evaluate antibiotic use in patients with typhoid fever using the Gyssens method at TK IV 02.07.04 Hospital, Bandar Lampung, in 2023.

2. Method

This study employed an analytical observational design with a cross-sectional approach to describe the qualitative analysis of antibiotic use in patients with typhoid fever using the Gyssens method at TK IV 02.07.04 Hospital, Bandar Lampung, in 2023. The study sample consisted of medical records of typhoid fever patients treated at TK IV 02.07.04 Hospital in 2023 that met the inclusion criteria. Purposive sampling was applied, whereby samples were deliberately selected according to predefined inclusion criteria. Data were collected cross-sectionally from patients' medical records [7].

The inclusion criterion was patients diagnosed with typhoid fever, with or without comorbidities. The collected medical record data were processed and analyzed using the Gyssens method, which classifies antibiotic use into categories 0–VI. Following data processing, further data analysis was conducted.

Ethical approval for this study was obtained from the Health Research Ethics Committee of Universitas Malahayati (Approval No. 422/EC/KEP-UNMAL/IV/2024). Data analysis was performed descriptively to assess the profile of antibiotic use among typhoid fever patients at TK IV 02.07.04 Hospital, Bandar Lampung, by grouping, recording, and analyzing antibiotic therapy data. The collected medical records were evaluated for the appropriateness and rationality of antibiotic use according to the Gyssens flowchart in patients with typhoid fever during the 2023 study period. All data were analyzed using Microsoft Excel.

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3. Result and Discussion

A total of 121 medical records were included as study samples. Data extracted from the medical records comprised patient initials, medical record numbers, age, diagnosis, body weight, type of antibiotic prescribed, dosage, and timing of antibiotic administration. Furthermore, the antibiotic use profiles of hospitalized patients diagnosed with typhoid fever were evaluated using the Gyssens method.

Table 1. Patient Characteristics in Typhoid Fever Cases

Characteristics		**Total (n)**	**Percentage (%)**
Antibiotic	Ceftriaxone	121	100
Sex	Male	86	71
	Female	35	29
Age	14-19	21	17
	20-35	100	83
Weight	40-60 kg	37	31
	61-90 kg	84	69
Dosage	1 gram every 24 hour	3	2
	1 gram every 12 hour	118	98
Duration	3-4 days	29	24
	5-6 days	92	76

Regarding gender as a risk factor, typhoid fever may occur in both males and females at comparable rates. However, personal and food hygiene practices are often associated with gender-related behavioral patterns. Contamination with *Salmonella typhi* commonly occurs in unhygienic environments and through unsafe water sources, which serve as the primary modes of transmission for this bacterium. Irregular eating habits and the consumption of unhygienic food significantly increase the risk of developing typhoid fever [11].

In this study, patient characteristics were analyzed based on three variables: gender, age, and body weight. Of the 121 medical records reviewed, 71% of patients were male and 29% were female. These findings are consistent with previous studies reporting a higher prevalence of typhoid fever among male patients. One study noted that the majority of typhoid fever cases occurred in males [10]. Males tend to engage more frequently in outdoor activities, which increases their exposure risk to *Salmonella typhi*, for example through the consumption of contaminated food or beverages. In contrast, females generally exhibit greater attention to personal and environmental hygiene, potentially reducing their risk of infection. Increased outdoor activities among males, including the consumption of food and drinks contaminated with *Salmonella typhi*, represent a major transmission route for typhoid fever [10].

Based on age distribution, 17% of patients were aged 14–19 years, while 83% were aged 20–35 years, according to medical record data from typhoid fever patients treated in 2023 at TK IV 02.07.04 Hospital, Bandar Lampung. The highest prevalence was observed among individuals in the productive age group, which may be attributed to increased outdoor activities and work-related exposure, thereby elevating the risk of infection [10].

Empirical antibiotic therapy in this study followed the Indonesian Ministry of Health Regulation No. 28 of 2021 concerning Guidelines for Antibiotic Use. According to these guidelines, the most common causative agents of typhoid fever are *Salmonella typhi* and *Salmonella paratyphi* A, B, and C. Ceftriaxone administered intravenously is recommended as a third-line treatment option, with a dosage of 1 g every 12 hours for adults, and 25–50 mg/kg body weight every 12 hours for pediatric patients. The recommended duration of antibiotic therapy is until the patient has been afebrile for at least five days, with a maximum treatment duration of 14 days.

Ceftriaxone was prescribed in 100% of the 121 medical records reviewed for typhoid fever patients treated in 2023 at TK IV 02.07.04 Hospital, Bandar Lampung. According to the Ministry of Health guideline

No. 28 of 2021, ceftriaxone is categorized as a third-line antibiotic option for typhoid fever treatment. Ceftriaxone belongs to the third-generation cephalosporin class, along with cefotaxime, cefixime, and cefoperazone [10]. Cephalosporins are broad-spectrum β-lactam antibiotics that exert their antibacterial effect by inhibiting microbial cell wall synthesis. Ceftriaxone offers several advantages, including a lower rate of resistance and fewer adverse effects. Clinical improvement, particularly defervescence, typically occurs by the fourth day of therapy, and blood culture results often become negative by the same time point, allowing for a shorter duration of treatment. Ceftriaxone is widely preferred in the management of typhoid fever due to its longer half-life of approximately eight hours, compared to cefotaxime, which has a half-life of approximately one hour, resulting in more prolonged antibacterial activity. Furthermore, ceftriaxone demonstrates higher effectiveness against Gram-negative bacteria, including *Salmonella typhi*, through stronger inhibition of bacterial cell wall synthesis, and has a lower resistance rate compared to cefotaxime [10].

Table 2. Gyssens Evaluation

Antibiotic	Category (Gyssens flowchart)												Total
	VI	V	IV				III		II		I	0	
			A	B	C	D	A	B	A	B			
Ceftriaxone (n)	0	0	0	0	0	0	0	29	1	0	0	91	121
Percentage (%)	0	0	0	0	0	0	0	24	1	0	0	75	100

Other study indicated that ceftriaxone was prescribed to 28 patients (68.3%) in patients with pneumonia, whereas cefotaxime was administered to 13 patients (31.7%). Ceftriaxone demonstrated the highest Defined Daily Dose (DDD), reaching 25.54 DDD per 100 patient-days, while cefotaxime showed a substantially lower value of 5.15 DDD per 100 patient-days. The peak utilization of both antibiotics was observed in November 2022, with ceftriaxone accounting for 90% of the Drug Utilization (DU) segment and cefotaxime representing the remaining 10%. Qualitative assessment using the Gyssens method revealed that antibiotic use was considered rational in 16 patients (39%), whereas 25 patients (61%) received antibiotics for an insufficient duration [13].

The duration of antibiotic therapy was 3–4 days in 24% of patients and 5–6 days in 76% of patients, based on 121 medical records. According to the Indonesian Ministry of Health Regulation No. 28 of 2021 on antibiotic therapy for typhoid fever, one of the recommended treatments is ceftriaxone, with a treatment duration until the patient has been afebrile for at least five days. Antibiotic use for more than seven days should be accompanied by peripheral blood smear morphology examination. Therefore, the administration of ceftriaxone for less than five days can be considered irrational due to an excessively short duration of therapy based on the guideline.

Regarding dosing frequency, 2% of patients received ceftriaxone at a dose of 1 g once daily, while 98% received 1 g twice daily. According to the Ministry of Health Regulation No. 28 of 2021, ceftriaxone for typhoid fever should be administered intravenously at a dose of 1 g every 12 hours or 2 g every 24 hours. Thus, the administration of ceftriaxone at a frequency of 1 g once daily is classified as irrational according to the guideline [9].

Based on the evaluation of antibiotic use using the Gyssens method, among the 121 medical records of typhoid fever patients treated in 2023 at TK IV 02.07.04 Hospital, Bandar Lampung, 75% of antibiotic use was categorized as rational (category 0), while the remaining 25% was classified as irrational (categories I–VI). According to the Ministry of Health Regulation No. 28 of 2021, antibiotic therapy for typhoid fever caused by *Salmonella typhi* is recommended to continue until the patient has been afebrile for five days. Based on the Gyssens evaluation, ceftriaxone use for less than five days was therefore considered irrational and classified under category IIIB, accounting for 24% of cases, indicating an excessively short duration of therapy. In addition, this study identified irrational antibiotic use related to dosing, specifically intravenous ceftriaxone administered at a frequency of 1 g once daily. Based on the ceftriaxone dosing recommendations

in the Ministry of Health Regulation No. 28 of 2021, this practice was classified as irrational and categorized as Gyssens category IIA, accounting for 1% of cases, indicating inappropriate dosage [8][9].

5. Conclusion

Most ceftriaxone use in hospitalized typhoid fever patients was appropriate according to the Gyssens method. Nevertheless, inappropriate use remained evident, particularly due to excessively short treatment duration and suboptimal dosing frequency. Strengthening adherence to national antibiotic guidelines and routine prescription audits is necessary to improve antibiotic stewardship in hospital practice.

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Conflict of Interest
None declared

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