EVALUATION OF INTRAVENOUS ANTIBIOTIC USE IN PEDIATRIC PNEUMONIA PATIENTS USING ATC/DDD AND GYSSENS METHODS AT PRIMAYA HOSPITAL SEMARANG

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INTISARI

Kasus anak-anak yang mengalami Bronkopneumonia, angka resistensi antibiotik meningkat akibat penggunaan antibiotik yang tidak tepat. Penelitian ini bertujuan untuk mengevaluasi penggunaan antibiotik intravena pada pasien pneumonia anak. Penelitian berlangsung secara retrospektif dengan analisis metode *Anatomical Therapeutic Chemical/Daily Defined Dose* dan Gyssens. Pengumpulan data berlangsung di di Rumah Sakit Primaya Kota Semarang. Subyek yang terlibat dalam penelitian ini mencakup seluruh pasien anak-anak yang menjalani rawat inap dan memperoleh peresepan antibiotik intravena pada tahun 2023. Hasil penelitian menunjukkan bahwa antibiotik Seftriakson diresepkan pada 28 pasien (68,3%) dan Sefotaksim pada 13 pasien (31,7%). Peresepan Seftriakson memiliki nilai DDD tertinggi 25,54 DDD/100 hari sedangkan sefotaksim memiliki nilai terendah 5,15 DDD/100 hari. Puncak peresepan terjadi pada November 2022, Seftriakson termasuk dibagian segmen DU 90% dan Sefotaksim pada segmen DU 10%. Hasil evaluasi dengan metode Gyssens menunjukkan 16 pasien (39%) yang masuk dalam kategori rasional dan sebanyak 25 pasien (61%) masuk dalam kategori pemberian terlalu singkat

Kata kunci: *Bronkopneumonia, Antibiotik, ATC/DDD, DU 90%, Gyssens.*

ABSTRACT

In the case of children with bronchopneumonia, the rate of antibiotic resistance is increasing due to the inappropriate use of antibiotics. This study aims to evaluate the use of intravenous antibiotics using Geyssens and ATC/DDD and DU 90% combination approaches in pediatric pneumonia patients. The study was held retrospectively by analyzing the Anatomical Therapeutic Chemical/Daily Defined Dose and Gyssens methods. Data collection was held at Primaya Hospital, Semarang City. Subjects involved in this study included all pediatric patients who were hospitalized and prescribed intravenous antibiotics in 2023. The results showed that Ceftriaxone antibiotics were prescribed in 28 patients (68.3%) and Cefotaxime in 13 patients (31.7%). Ceftriaxone prescribing had the highest DDD value of 25,54 DDD/100 days, while cefotaxime had the lowest value of 5,15 DDD/100 days. The highest use of these antibiotics occurred in November 2022; Ceftriaxone was included in the 90% DU segment, and Cefotaxime was included in the 10% DU segment. The results of the qualitative Gyssens method evaluation were that 16 patients (39%) were rational, and 25 patients (61%) were too short in administration.

Keywords: *Bronchopneumonia, Antibiotics, ATC/DDD, DU 90%, Gyssens.*

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INTRODUCTION

Inflammation of the lung parenchyma, which includes the alveolus and interstitial tissue, is caused by pneumonia, an airway infection. Pneumonia is typically characterized by coughing, wheezing, fever, wet rales, and the presence of infiltrates on a thoracic X-ray. Among the 156 million cases of pneumonia reported in children under five worldwide, 74% (approximately 115.3 million cases) were documented in the 15 countries with the highest incidence rates. Notably, just six countries accounted for over half (44%) of all pneumonia cases among children globally. In 2019, there were a total of 800,000 cases of childhood pneumonia, with the majority occurring in children under 5 years of age (Farah et al., 2021).

According to a study conducted by Yusuf et al. (2022), the evaluation results of antibiotics for pneumonia qualitatively using the Gyssens method showed that 6% were classified as category alternative as more effective, 6% were category given for too long, and 2% were category incorrect dosage. It was concluded that the use of antibiotics in Surabaya Teaching Hospital is still not appropriate. In line with previous study, Yanti (2016) revealed the quality of antibiotic use at RSUD Sultan Syarif Mohamad Alkadrie Pontianak from July to June 2015 using the Gyssens method on 18 pediatric pneumonia patients indicated that antibiotic usage fell category alternative more effective 5.56%, category alternative more affordable 2.78%, category inappropriate dosage 50.01%, and category inappropriate dosing interval at 41.67%. This suggests that the antibiotic utilization at RSUD Sultan Syarif Mohamad Alkadrie remains improper.

In a study conducted by Hanifah et al. (2022), it was explained that antibiotic evaluation using the ATC/DDD and DU 90% methods in the internal medicine ward of a private hospital in Bandung City revealed a total DDD/100 bed-days value of 144.58 for all antibiotic uses. The highest DDD value was for levofloxacin at 48.83, which falls under the DU90% category, followed by Azithromycin, Cefixime, Ceftriaxone, Meropenem, and Moxifloxacin. Another study by Prasetyo EY & Kusumaratni DA (2018) explains that the use of antibiotics in pediatric patients diagnosed with pneumonia at Kediri City Hospital showed the highest DDD/100 bed-days for Ceftiaxone (23.86), Ceftazidime (11.16), Cefoperazone (5.81), Azithromycin (3.72), Levofloxacin (2.79), Cefotaxime (2.23), Ampicillin-Sulbactam (0.78). Antibiotics included in the DU90% segment are Ceftriaxone, Ceftazidime, Cefoperazone, and Azithromycin.

Patients with pneumonia can be treated with antibiotics. Treatment is definitive when the bacteria causing pneumonia are known or empirical when the culture procedure is still pending. Increasing resistance to antibiotics commonly used as empirical treatment by doctors can reduce the effectiveness of pneumonia treatment owing to the relatively high use of antibiotics (Anggraini, 2021). Antibiotic resistance can also result in misuse and irrational use of drugs (Mahmudah et al. 2016). Based on the previous description, the appropriateness of antibiotic use is still carried out separately, both qualitative and quantitative. It is important to evaluate intravenous antibiotics using Geyssens, ATC/DDD, and DU 90% approaches.

METHODS

Data were collected retrospectively at Primaya Hospital in Semarang City from January to December 2022 for this descriptive observational study. A total of 53 patients were included in the study population. Forty-one patients who met the inclusion criteria were identified during data collection in June. These criteria included pediatric patients aged 0 to 5 years who were diagnosed with pneumonia, received antibiotics via intravenous route, and patients who had complete medical

records (patient name, patient age, gender, drug data, duration of administration, length of hospitalization (LOS), and route of administration. Patients died during data collection (The patient died due to other diseases, and the required supporting data, such as lab data, was inadequate for the evaluation of antibiotic administration), and patients who were transferred to another hospital or did not receive antibiotics were excluded from the study.

Qualitative analysis was conducted by documenting all types of intravenous antibiotics used in hospitals for pediatric pneumonia therapy. The antibiotic usage data was then compared with consensus or guidelines for pediatric pneumonia therapy, such as the Pediatric Community Guideline (2011), The World Health Organization (2023), and Pedoman Penggunaan Antibiotik Kementrian Kesehatan Republik Indonesia (2021). The data was analyzed based on indications, potential, toxicity, cost, and availability of administration duration, dosage, interval, route, and timing (Yusuf et al., 2022). Subsequently, it was categorized into 0 - VI according to the Geyssens flowchart from Ian MG (2008).

To characterize data from medical records and perform quantitative analysis, the DDD and DU 90% methods are used to determine the number of antibiotics used by pediatric pneumonia patients in 5 steps: a). Classification of ATC codes for pneumonia based on WHO guidelines (link available on: https://atcddd.fhi.no/atc_ddd_index/); b). Identifying the WHO Standard DDD in grams; c). Drug utilization in DDD was calculated using a formula = **Duration of AB therapy/DDD WHO X Antibiotic dosage (gram)**, d). The DDD/100 bed days' value is calculated using the formula = **Total usage antibiotics/WHO standard (gram) X 100/ Total Length of stay (LOS)**; e). Finally, the DU 90% score is calculated using the formula = **DDD per 100 bed days/Total DDD per 100 bed days X 100%.**

Excel and SPSS were used for data processing. This study obtained ethical approval from STIKES Telogorejo Semarang with reference number 091/VI/KE/STIKES/2023. The selection of data criteria can be seen in **Figure 1**.

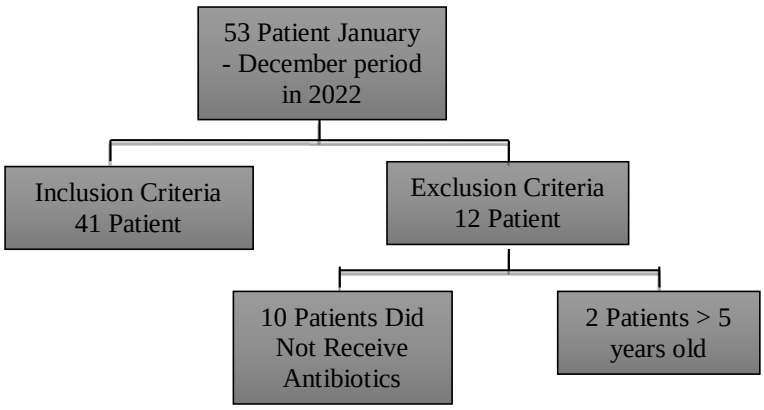

Figure 1. Inclusion and Exclusion Criteria Chart

RESULTS AND DISCUSSION

The results of patient characteristics and antibiotic use profiles are displayed by gender; it can be seen that male patients slightly outnumber female patients with a ratio of 51.2% versus 48.8%. This observation could be attributed to various factors, such as differences in outdoor activities between males and females, which may lead to varied exposure to germs causing respiratory or other diseases. Cultural and societal factors may also play a role in these gender-based differences/ Parents of boys may perceive themselves as physically stronger and, therefore, more protective of their daughters, which could lead to girls spending more time at home (Nelita et al., 2022). This finding is in line with research conducted by Sangadji NW et al. (2022) at the Cibodasari Health Center, which similarly found a higher number of male toddlers (56.0%) compared to female toddlers (44.0%).

Children under five years old are susceptible to pneumonia, which is characterized by symptoms such as coughing and shortness of breath. Pneumonia predominantly affects the age group. Partly due to their weaker immune systems making them more susceptible to airborne diseases (Farida et al. 2017). Research by Norcahyanti et al. (2021) showed that the age range of 1 to 24 had the highest risk of pneumonia (52.2%) in Bangil Regional General Hospital, totaling 402 pediatric inpatients. This report contrasts with a study conducted by Inez et al. (2019) at Tanjungpura University Hospital, which identified an age group of 5 to 11 years as the most affected by pneumonia, involving 63 patients.

Most commonly, ceftriaxone (68.3%) is this antibiotic administered to pediatric pneumonia patients. Research conducted by Kaal et al. 2024 found that intravenous ceftriaxone is highly effective, with a success rate of 96.2%, compared to oral amoxicillin/clavulanic acid, which had a lower success rate of 76.2%. Another study from Gums et al. (2018) stated that Streptococcus pneumoniae bacteria are consistently more susceptible to ceftriaxone. This is because cefotaxime has a short half-life of about one hour), leading to larger fluctuations in drug concentrations, which can make it harder to maintain the necessary antibiotic levels for effective treatment.

The chosen route of administration is intravenous (iv) administration, which is based on the site of infection and its effectiveness. Intravenous antibiotics are typically administered to patients with moderate to severe infections. In addition, intravenous treatment is necessary in cases where the patient is unresponsive, unable to swallow, dehydrated, or in shock. This allows antibiotics to be delivered to affected tissues directly into the systemic circulation (Rachmawati et al. 2020), This finding aligns with the statement of Mathur S et al. (2018), which states that intravenous dosage forms accelerate the onset of the therapeutic effect, especially for patients admitted to the hospital, with symptoms such as shortness of breath.

Table I. Patient Characteristics and Antibiotic Use Profile

Description		Total (N=41)	Percentage (%)
Patient Characteristics			
Gender	Male	21	51,2
	Female	20	48,8
Age (Years)	Mean ±SD	29,17±17,99	
	0-1	19	46,3
	2-3	13	31,7
	4-5	9	22
Treatment Status	BPJS	17	41,5
	General	9	22
	Other Insurance	15	36,6
Antibiotics Use Profile			
Types of Antibiotics	Ceftriaxone	28	68,3
	Cefotaxime	13	31,7
Antibiotics Group	Cephalosporins	41	100
Administration Route	Intravenous	41	100
Ceftriaxone Dossage (mg)	Mean ±SD	632,14±137,58	
	<500	12	29,3
	>500	16	39
Cefotaxime Dossage (mg)	Mean ±SD	380,77±164,30	
	<500	11	26,8
	>500	2	4,9
Frequency of Administration (hours)	8	14	34,1
	12	21	51,2
	24	6	14,6
Duration of Therapy (Days)	Mean ±SD	2,51±1,31	
	1-3	31	75,6
	4-7	10	24,4
Total LOS (Days)	156	3,80 (±49,12)	

The total LOS for pneumonia patients was 156 days, with an average of 3.80 days, indicating that they spent approximately 3 to 4 days in the hospital. The severity of the disease, concomitant disorders, and clinical condition of the patients could have influenced the lower LOS. The findings of this study are in line with the study conducted by Azyenela et al. (2022) at Solok City Hospital, in which the average length of stay also ranged from 3 to 4 days.

Antibiotic Use Profile Based on DDD/100 Days Value

The use of ceftriaxone antibiotics was higher, with a DDD value of 8,782 DDD, compared to the WHO standard of 2 g (Figure 2) (Figure 3). The high use of ceftriaxone may be due to the large number of hospitalized patients, the high number of pneumonia cases in November, and the administration of ceftriaxone antibiotics as the first line of therapy for hospitalized pediatric pneumonia patients.

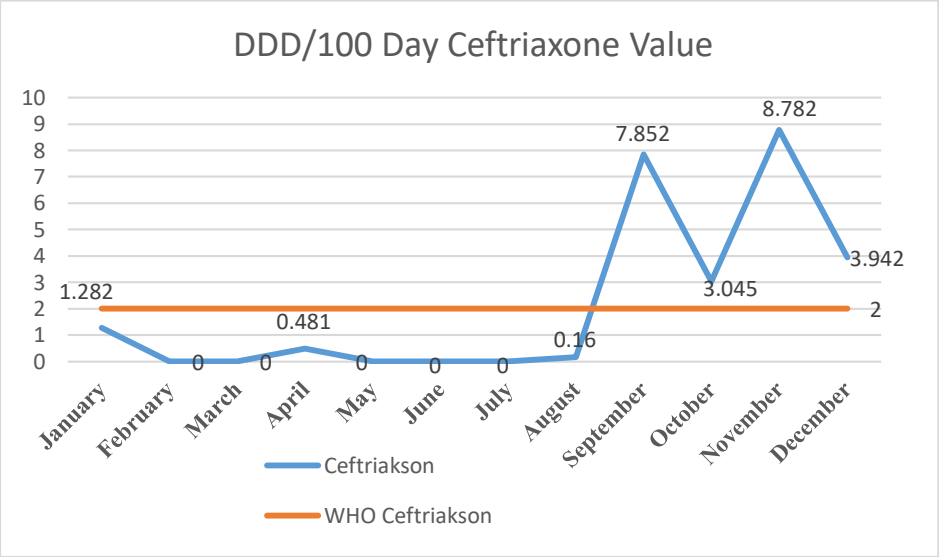

Figure 2: Graph of Ceftriaxone DDD Value per month

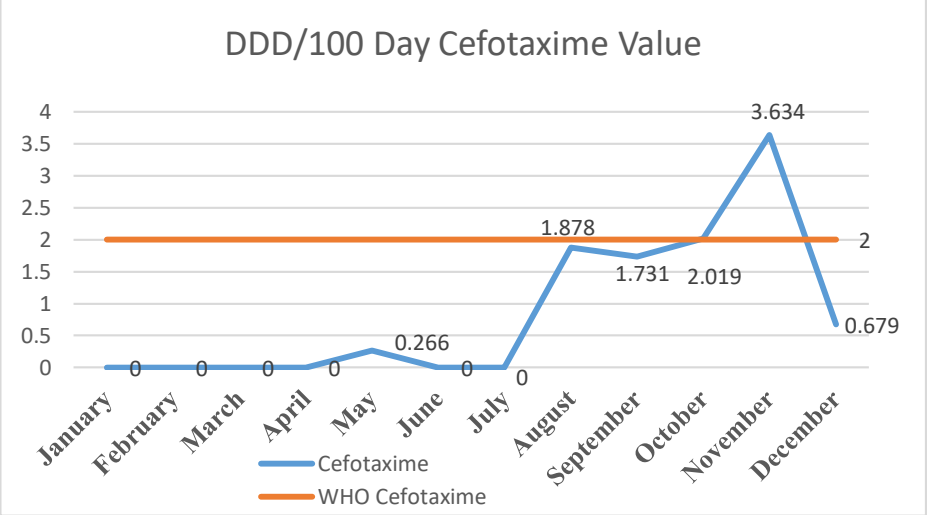

Figure 2: Graph of Cefotaxime DDD Value per month

This study is comparable to that conducted by Wahyudi A. & S. Pertiwi (2022) at Sultan Agung Semarang Hospital, with the results of the highest use of ceftriaxone antibiotics in March 2021, amounting to 0.31 DDD/100 days among the population of 34 patients. However, different results were carried out (Park J et al. 2017) in South Korea with a total of 50 patients and obtained the highest number of antibiotics used. In that study, the highest antibiotic usage was attributed to a combination of penicillins (2,367 DDD/100 days) because these antibiotics include a broad spectrum that doctors widely prescribe.

Table II. Calculation of DDD and DU 90% Value

Code ATC	Name Of Antibiotics	Route	DDD standard WHO (gram)	Amount Of Antibiotics (gram)	Total LOS (Day)	DDD 100/Day Inpatient	DU (%)	DU Cumulative	Segment DU
J01DD04	Ceftriaxone	i.v	2	79,7	156	25,54	83,22	83,22	90 %
J01DD01	Cefotaxime	i.v	4	32,11		5,15	16,78	100	10%
Total						**30,69**			

The total DDD value was 30.69 DDD/100 days of hospitalization, with the use of ceftriaxone having the highest DDD value of 25.54 DDD/100, while Cefotaxime had the lowest DDD value of 5.15 DDD/100 days. Ceftriaxone is used more frequently than other third-generation Cephalosporins due to its mechanism of action, which inhibits microbial cell wall synthesis. The inhibition of cell wall formation also hinders transpeptidase enzymes and the long half-life of ceftriaxone, which allows twice- or even once-daily dosing in many situations, which can result in cost savings and improved treatment effectiveness (Dewi TP & Dhirisma F, 2021). This finding is in accordance with research conducted by F Rukminingsih & A Apriliyani (2021) at the St Elisabeth public-private hospital Semarang, which found that Ceftriaxone antibiotics had the highest DDD value per 100 days of hospitalization (15,10 DDD/100 days), while Cefotaxime antibiotics had the second DDD highest value (1,49 DDD/100 days) follows another antibiotic such as Cefixime, Ceftazidime, Amoxicillin, Ampicillin, Thiamphenicol and Meropenem.

Ceftriaxone (83.22%) falls into the 90% DU category, while cefotaxime (16.78%) is an antibiotic that belongs to the 10% DU segment. Antibiotics classified under the 90% DU category are usually prescribed, whereas those in the 10% DU segment are occasionally prescribed for pneumonia. Due to the potential for antibiotic resistance, prescribing antibiotics in the 90% DU category must be controlled.

The Rationality of Antibiotic Use Based on Gyssens Method

Out of the 41 prescriptions in our study, 16 (39%) were classified as appropriate/rational category (category 0) according to the Gyssens method. Category 0 indicates complience antibiotic therapy regimens with treatment guidelines and the accuracy of the diagnosis of Bronchopneumonia or pediatric pneumonia made by medical personnel in the inpatient room of Primaya Hospital Semarang City. The evaluation findings also showed that category III treatment included inappropriate treatment. Specifically, 25 out of the 41 prescriptions (61%) which was related to the appropriateness of too short a duration of antibiotic administration (Table III).

When patients are allowed to continue the therapy outpatient antibiotic prescriptions, there is a risk of inappropriate antibiotic duration. Using antibiotics for a shorter duration than recommended can result in treatment failure and the development of resistant bacteria to these antibiotic drugs, even riskier if there are negative side effects of the drug (GR Al Farizi et al., 2021; F Nugroho et al., 2011; PN Risalati et al., 2022). These findings contrast with the research of Rahayu YD et al. (2014), which revealed information on the use of antibiotics for 3 to 5 days (80.2%) and 6 to 10 days (17.6%).

Table III. Results of Rationality of Antibiotic Use Based on the Gyssens Method

No	Category Gyssens	Description	Number of Cases	Percentage (%)
1	Antibiotic category 0 (appropriate)	Appropriate	16	39%
2	Antibiotic category I (not timely)	-	-	-
3	Antibiotic category IIa (inappropriate dose)	-	-	-
4	Antibiotic category IIb (inappropriate interval)	-	-	-
5	Antibiotic category IIc (inappropriate route)	-	-	-
6	Antibiotic category IIIa (too long use)			
7	Antibiotic category IIIb (too short of use)	Inappropriate	25	61%
8	Antibiotic category IVa (More effective antibiotic needed)	-	-	-
9	Antibiotic category IVb (less toxic alternative)	-	-	-
10	Antibiotic category IVc (cheaper alternative)	-	-	-
11	Antibiotic category IVd (narrower alternative spectrum)	-	-	-
12	Antibiotic category V (no indication)	-	-	-
	Antibiotic category VI (incompleted data)	-	-	-
	Total		**41**	**100**

The duration of antibiotic treatment for the patient's condition also affects how long antibiotics are given to patients with pneumonia. Antibiotics can be stopped within 3 to 5 days for patients without immunodeficiency or structural respiratory disease. Patients with immunodeficiency and/or structural respiratory disease may discontinue antibiotics within 7 days. In case of poor clinical response or severe immunodeficiency, antibiotics may be discontinued within 10 to 14 days or longer (Yaremchuk et al., 2015). Based on the evaluation results, none of the patients had significant severity of illness or other health problems or complications. Therefore, the Kementrian Kesehatan Republik Indonesia (2021) in antibiotics for pediatric pneumonia for a duration of 3 to 5 days, depending on the clinical condition of the patient.

The results of a 2022 evaluation of high-risk category IIIb inpatients at Primaya Semarang Hospital revealed irrational antibiotic use. Establishing guidelines for antibiotic use in hospitals is essential to ensure that all medical staff adhere to the same standards when prescribing antibiotics for urgently needed treatment. To guarantee that prescribed antibiotics are highly appropriate for the patient's condition and illness, a bacterial culture must also be performed before deciding on the mode of administration (Sonia et al., 2023)

CONCLUSION

This study showed Ceftriaxone had the highest antibiotic utilization rate, with a DDD value of 25.54 DDD per 100 days. Cefotaxime was less commonly used, with a DDD value of 5.15 DDD per 100 days. Ceftriaxone and cefotaxime are antibiotics in the 90% DU and 10% DU segments, respectively. It is desirable to conduct research involving more than two types of antibiotics or various groups, incorporate data from two to three additional years for comparison, and perform a cost-effectiveness analysis or investigate treatment costs.

The use of antibiotics in pediatrics diagnosed with pneumonia at Primaya Hospital Semarang City in 2022, adjusted based on the Antibiotic Use Guideline, was deemed appropriate. Category IIIb indication too short a duration of antibiotic use with 25 patient cases (61%), compared to the rational category with 16 patient cases (39%).

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