

Quantitative Evaluation of Antibiotic Prescribing in Dengue Patients: Application of the ATC/DDD Method at HKBP Hospital

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ABSTRACT

Infectious diseases, including those caused by pathogenic bacteria, remain a major health concern worldwide. The widespread use of antibiotics in treating infectious diseases increases the risk of irrational prescribing, potentially leading to suboptimal therapeutic outcomes. This study aims to evaluate antibiotic utilization based on patient characteristics, antibiotic usage profiles, and the quantity of antibiotic consumption in Defined Daily Dose (DDD) units among hospitalized patients at HKBP General Hospital diagnosed with dengue fever. This was an observational, retrospective study using secondary data extracted from the Hospital Information System (SIRS) for the period of January to April 2024. Collected data included drug names, dosage forms and strengths, total quantities used, number of hospitalized patients per month, and duration of hospital stay. Data analysis employed the Anatomical Therapeutic Chemical (ATC)/DDD methodology and the Drug Utilization 90% (DU90%) approach. The findings showed that two types of antibiotics were prescribed for dengue fever patients during the study period, with an average total consumption of 280.07 DDD/100 patient-days. The most frequently used antibiotics were cefixime (66.70%) and cefotaxime (33.30%). Intravenous administration was the predominant route, and the majority of patients (85.71%) received antibiotic therapy for less than 3 days. These results highlight the need for continuous monitoring of antibiotic use to ensure rational prescribing practices in hospital settings.

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1. INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus (DENV). The dengue virus is transmitted to humans through the bite of infected female mosquito vectors, especially mosquitoes of the *Aedes aegypti* and *Aedes albopictus* species. The incubation period of the dengue virus in the human body until symptoms appear ranges from 3-10 days after a mosquito bite, with an average incubation period of 5-7 days. Common symptoms experienced by dengue sufferers are fever for 2-7 days, accompanied by several signs of severe headache, pain behind the eyes, muscle and joint pain, rash, nausea, vomiting, and minor hemorrhagic manifestations or positive tourniquet test results.

Dengue fever can develop into a severe condition that causes complications and even has the potential to cause death. The incidence of dengue fever cases continues to experience a sudden high increase, even resulting in major outbreaks. This has led to dengue fever being considered a severe public health emergency. CDC explains that around 40% of the world's population lives in areas endemic for dengue fever. Every year there are 390 million dengue virus infections, 96 million of which are clinically manifested. The highest cases globally were in 2019. Dengue cases occurred in all regions and transmission occurred for the first time in Afghanistan. The incidence of dengue fever is endemic in more

than 100 tropical and subtropical countries. The impact is more severe in the Americas, Southeast Asia, and the Western Pacific. Asia represents up to 70% of the global disease burden.

A major dengue fever outbreak occurred in Southeast Asia and China in 2014 and in America in 2016. In 2020, there was an increase in the number of dengue fever cases in several Asian countries such as Bangladesh, India, Nepal, Yemen, Maldives, Sri Lanka, Singapore, Thailand, Timor Leste, and Indonesia. Reported from The Asean post, the highest number of dengue fever cases in the ASEAN region in 2019 was in the Philippines with 414,532 cases, Indonesia with 110,000 cases, and Laos with 38,000 cases. According to the North Sumatra Provincial Health Office, cumulatively from January to September 2022 the number of dengue fever (DBD) sufferers in this area reached 5,270 cases. Head of the North Sumatra Health Office Ismail Lubis said that of the 5,270 dengue fever sufferers, 24 of them died.

Hospitals are health service institutions for the community with the aim of improving services that are more qualified and affordable for the community, in order to realize the highest level of health. Hospital Pharmacy Installation (IFRS) is a functional implementing unit that organizes all pharmaceutical service activities in hospitals. Pharmaceutical services in hospitals are an inseparable part of the hospital health service system that is oriented towards the management of pharmaceutical supplies, medical devices, and disposable medical materials that are quality and affordable for all levels of society including clinical pharmacy services. High antibiotic use for infectious diseases increases the risk of irrational antibiotic use which can result in the therapeutic goal not being achieved. Another study found that around 40-62% of antibiotics are used irrationally, including for diseases that do not actually require antibiotics. One of the consequences of irrational antibiotic administration is that it can cause bacteria to become resistant to antibiotics. Resistance causes an increase in the number of deaths and economic burden, due to the extension of the length of hospitalization, the use of antibiotics is more expensive and longer. Deaths due to resistance are estimated to reach around 700,000 people.

Evaluation of antibiotic use is one of the indicators of the quality of the irrationality control program. Evaluation of antibiotic use can be carried out using qualitative methods to assess the rationality of antibiotic use. One of the evaluation methods that can be used is the Gyssens method, which can assess the rational use of antibiotics (category 0) and irrational antibiotic users (categories I-IV). Based on a preliminary study that has been conducted according to data taken from the HKBP Balige Hospital, dengue fever is a disease that is mostly found in the HKBP Balige Hospital. From the data taken from the period January-April 2024, there were 50 cases of dengue fever patients who had been treated at the HKBP Balige Hospital Inpatient Installation. Based on these data, researchers are interested in conducting a study entitled Evaluation of Antibiotic Use in Dengue Hemorrhagic Fever (DHF) Patients Using the ATC/DDD Method in the HKBP Balige Hospital Inpatient Installation for the Period January-April 2024.

2. RESEARCH METHOD

This study employed an observational (non-experimental) design with a quantitative approach, aiming to analyze the characteristics of antibiotic use among dengue fever patients and to quantify antibiotic consumption using the Defined Daily Dose (DDD) methodology. The research design was cross-sectional, utilizing retrospective data collected from inpatient prescription records at HKBP Balige General Hospital over the period of January to April 2024. The sampling technique used in this study was stratified random sampling, allowing for representative selection from the population by dividing it into homogenous subgroups (strata) based on relevant characteristics. This approach ensured that each stratum was adequately represented in the sample. Data were retrieved from patient medical records and included information on prescribed antibiotics, dosage forms, strengths, administration routes, quantity used, patient demographics, and duration of hospitalization. Following the screening and validation of prescription records, a total of 35 eligible medical records were included in the final analysis. This number reflected the fact that not all hospitalized dengue fever patients received antibiotics during the study period, and several prescription records were excluded due to illegibility or incomplete data. Antibiotic utilization was measured using the WHO's ATC/DDD classification system, and drug consumption was expressed in DDD per 100 patient-days. The Drug Utilization 90% (DU90%) method was also applied to determine the most frequently used antibiotics.

3. RESULTS AND DISCUSSIONS

Evaluation of antibiotic use in terms of quantity is done by calculating using the DDD (Defined Daily Dose) value with the unit DDD/100 days of care (100 HR). Antibiotics used in hospitalized patients are

classified based on the ATC code, then the amount of strength is calculated by multiplying the quantity of drug use by the strength of the preparation in grams. Furthermore, the DDD of use is calculated by dividing the total amount of strength by the definitive DDD set by WHO. After that, the total DDD of use is divided by the number of days of patient care per month to obtain DDD/100 HR, which is the unit used in hospitalized patients. The data in this study were obtained from the medical records room at the HKBP Balige General Hospital.

The data obtained are in the form of drug names, dosage forms, dosage strengths, number of antibiotic uses each month, number of inpatients in January - April, average length of stay for patients each month January - April 2024. Based on the results of the medical record data search, it is known that the number of inpatients with dengue fever at the HKBP Balige General Hospital for the period January - April 2024 was 50 patients. Dengue fever patients who received single and combination antibiotics were 35 patients and the rest were patients who did not receive antibiotic therapy, so the research sample that could be evaluated was 35 patients. The total length of hospitalization for all patients was 105 days. The characteristics of dengue fever patients who received antibiotics in the inpatient room of the HKBP Balige General Hospital can be seen in table I.

3.1. Characteristics of DHF patients receiving antibiotics

Table 1. Characteristics of dengue fever patients who received antibiotics in the inpatient room of HKBP Balige

Characteristics	Number of Patients	Percentage (%)
Age (Years)		
≤ 1	1	2,8
2-6	10	28,6
7-12	10	28,6
13-18	14	40
Total	35	100
Gender		
Laki-Laki	18	51,43
Perempuan	17	48,57
Total	35	100
Lama Rawat Inap (Hari)		
≤ 3	30	85,71
4 – 6	5	14,29
≥ 7	0	0
Total	35	100
Jenis Antibiotik		
Cefixime 50 mg	3	7,32
Cefixime 120 mg	1	2,43
Cefixime 200 mg	7	17,1
Cefixime 400 mg	1	2,43
Cefixime 450 mg	1	2,43
Cefotaxime 250 mg inj	2	4,88
Cefotaxime 300 mg inj	3	7,32
Cefotaxime 400 mg inj	3	7,32
Cefotaxime 500 mg inj	8	19,51
Cefotaxime 600 mg inj	2	4,88
Cefotaxime 1000 mg inj	10	24,39
Total	41	100

Based on Table I. it is known that dengue fever patients in the inpatient room of HKBP Balige Hospital in the period January-April 2024 who received the most antibiotics were in the age range of 13-18 years (40%). Dengue fever patients who received antibiotics in the inpatient room of HKBP Balige Hospital in the period January-April 2024 were mostly male (51.43%). The age of 13-18 years or referred to as teenagers is a stage of child development that already has more activities (Ministry of Health of the Republic of Indonesia, 2014). This is because adolescence is a period when they already have the freedom to choose the food they like and have activities outside the home, so that the nutritional status of teenagers can be disrupted due to children having difficulty eating.

The length of hospitalization for most patients (85.71%) was ≤ 3 days and the average length of hospitalization was 3 days. The most widely used type of antibiotic is Cefotaxime Injection 1000 mg (24.39%)(Ann et al., 2020). Cefotaxime is widely used as empirical therapy because it is a broad-spectrum antibiotic that is active against gram-positive and negative bacteria, as well as anaerobic bacteria. Cefotaxime has a relatively cheap price and relatively lower toxicity for pediatric patients compared to other types of antibiotics.

3.2. Antibiotic usage profile

Table II. List of Antibiotics Used in Dengue Fever Patients in the Inpatient Room of HKBP Balige General Hospital in 2024.

Pharmacology Major Group Code	Antibiotic Classes	Generic Name	ATC Code	definitive DDD (g)
J01D	Sefalosporin	Cefixime 50 mg	J01DD08	0,4
		Cefixime 120 mg	J01DD08	0,4
		Cefixime 200 mg	J01DD08	0,4
		Cefixime 400 mg	J01DD08	0,4
		Cefixime 450 mg	J01DD08	0,4
		Cefotaxime 250 mg inj	J01DD01	4
		Cefotaxime 300 mg inj	J01DD01	4
		Cefotaxime 400 mg inj	J01DD01	4
		Cefotaxime 500 mg inj	J01DD01	4
		Cefotaxime 600 mg inj	J01DD01	4
Cefotaxime 1000 mg inj	J01DD01	4		

Based on Table II, it shows that the number of antibiotics used in dengue fever patients at RSU. HKBP Balige in 2024 was 2 types of antibiotics included in the ATC code classification 'J', namely Antiinfectives for systemic use, including cefixime and cefotaxime. The ATC code listed in the table is used to group antibiotics with DDD values in grams (g). Table II also shows that the use of antibiotics in the Inpatient Room of HKBP Balige General Hospital is in accordance with the list of antibiotics listed in the 2024 National Formulary at level 3 health facilities.

A larger DDD/100 HR value illustrates a higher quantity of antibiotic use in 100 days of care. Conversely, a smaller DDD/100 HR value illustrates a lower quantity of antibiotic use, which means that doctors are more selective in prescribing antibiotics so that they can approach the principle of rational antibiotic use. The results obtained by researchers cannot be used to compare the level of selectivity of antibiotic use with other hospitals. This is due to differences in the time span used and differences in hospital types.

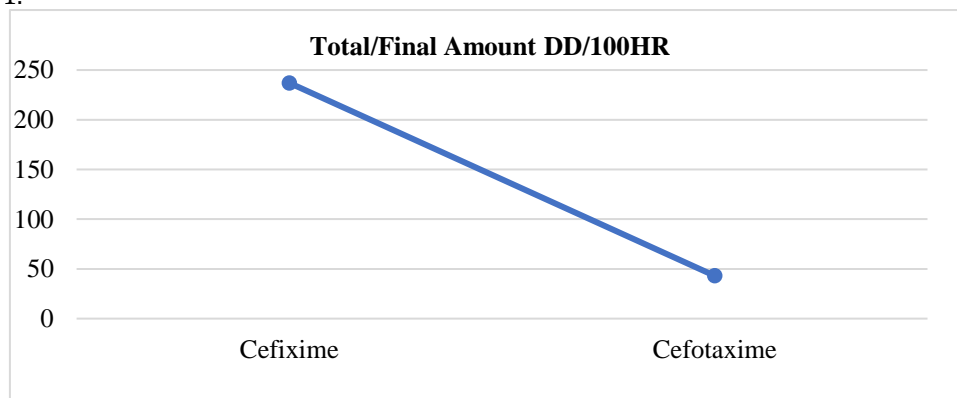
3.3. Total quantity of antibiotic use by antibiotic type in 2023

Table 3. Quantity of Antibiotic Use Per Month in the Inpatient Room of HKBP Balige General Hospital in 2024

Drug Name	Route of Administration	DDD/100 HR				Final	Amount Total	
		Januari	Februari	Maret	April			
Cefixime 50 mg	Oral	6,58	5,68	0,00	0,00	12,26	237,04	
Cefixime 120 mg	Oral	6,32	0,00	0,00	0,00	6,32		
Cefixime 200 mg	Oral	15,79	72,73	94,74	0,00	183,26		
Cefixime 400 mg	Oral	26,32	0,00	0,00	0,00	26,32		
Cefixime 450 mg	Oral	8,88	0,00	0,00	0,00	8,88	43,03	
Cefotaxime 250 mg inj	Parenteral	2,47	0,00	0,00	0,96	3,43		
Cefotaxime 300 mg inj	Parenteral	1,38	0,00	0,00	0,00	1,38		
Cefotaxime 400 mg inj	Parenteral	0,53	0,00	1,05	1,54	3,12		
Cefotaxime 500 mg inj	Parenteral	4,93	0,00	1,32	2,56	8,81		
Cefotaxime 600 mg inj	Parenteral	0,00	2,05	1,58	0,00	3,63		
Cefotaxime 1000 mg inj	Parenteral	1,32	9,09	2,63	9,62	22,66		
		74,52	89,55	101,32	14,68	280,07		280,07

Based on table 3, it is known that there are 2 types of antibiotics with different strengths used by dengue fever patients at HKBP Balige General Hospital during the period January - April 2024, with an average total DDD value / 100 patient-days of 280.07. These results are higher when compared to research conducted at Dr. Moewardi Hospital during the period of 2017, which was 111.87 DDD / 100 HR and research conducted on surgical patients at Dr. Slamet Martodirjo Pamekasan Hospital which was 72.12 DDD / 100 HR.

The following graph illustrates the total quantity of use of each antibiotic used in the Irna Anak Inpatient Room, Porsea Regional General Hospital in 2023 in DDD / 100 HR units which is shown in Figure 1.



Based on Figure 1, cefixime is the antibiotic with the highest DDD/100 HR value during 2024, which is 237.04. This can be interpreted that on average in 100 days of hospitalization at HKBP Balige General Hospital during 2024, there were around 13 patients who received cefixime therapy according to the WHO standard DDD, which is 0.6 grams per day. The DDD/100 HR value of cefixime is lower when compared to a study conducted on surgical patients at Dr. H. Slamet Martodirjo Pamekasan Hospital during the period January-March 2020 which showed the largest DDD/100 HR value, namely cefixime, of 34.50. Cefixime is widely used as empirical therapy because it is a third-generation cephalosporin antibiotic that has a broad spectrum against gram-positive and negative bacteria and anaerobic bacteria.

4. CONCLUSION

Based on the antibiotic evaluation study utilizing the ATC/DDD method at HKBP Balige General Hospital from January to April 2024, several conclusions can be drawn: First, in terms of patient characteristics, the highest proportion of antibiotic users were male patients (51.43%), with the 13–18 years age group (40%) being the most dominant among hospitalized dengue fever cases. This suggests a trend in antibiotic prescribing among adolescents, which may warrant further investigation into age-related prescribing behavior and clinical decision-making. Second, regarding the profile of antibiotic use, the most commonly prescribed antibiotic was Cefotaxime Injection 1000 mg, accounting for 24.39% of all antibiotics used during the study period. The intravenous route was the predominant mode of administration, aligning with hospital protocols for managing moderate to severe infections. Additionally, short-duration therapy was highly prevalent, with 85.71% of patients receiving antibiotics for less than three days. This could indicate either appropriate early de-escalation practices or potential overuse in non-bacterial conditions such as viral dengue, which requires further qualitative review. Third, the quantitative assessment using the ATC/DDD method showed that Cefixime had the highest usage level, with a total of 237.04 DDD/100 patient-days, exceeding the WHO-recommended threshold. This suggests a potential pattern of overutilization or inappropriate prescribing in cases where antibiotics may not be clinically indicated, particularly in viral infections like dengue fever. Such overuse contributes to the growing global threat of antimicrobial resistance (AMR), highlighting the need for stewardship interventions. Finally, based on the Drug Utilization 90% (DU90%) analysis, only two antibiotics—Cefixime and Cefotaxime—were found within the segment of drugs that made up 90% of total antibiotic consumption. The limited diversity of antibiotics used may reflect a restricted formulary or prescriber preference but could also indicate a lack of individualized antibiotic therapy based on

microbiological data. In conclusion, while the study provides valuable insights into antibiotic usage patterns in dengue fever patients, it also underscores the urgent need for enhanced antimicrobial stewardship programs, continuous monitoring of prescribing behavior, and improved diagnostic precision to ensure antibiotics are used rationally and effectively. Further research integrating clinical outcomes and bacterial culture results is recommended to validate and guide evidence-based prescribing practices.

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