



## EVALUATION OF THE RATIONALITY OF ANTIBIOTIC USE IN CHILD DIARRHEA PATIENTS IN THE INPATIENT CARE INSTALLATION

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### ABSTRACT

According to WHO and UNICEF, diarrheal disease occurs around 2 million cases and 1.9 million children die each year with a prevalence of 78% in developing countries. The treatment used is antibiotics. Irrational use of antibiotics can cause less effective treatment, decreased drug safety levels, high treatment costs and increased resistance. The purpose of this study was to evaluate the rationality of antibiotic use in pediatric diarrhea patients at UNS Hospital using the Gyssens method for the period January - September 2023. This study was conducted as an observational study with a descriptive design with retrospective sampling, the sample of this study was 80 patients and included in the inclusion category of 33 samples, then a descriptive analysis was carried out using the Gyssens assessment. The reference used is the Indian guidelines Academy of Pediatrics (IAP) 2022, DIH, MIMS, and UNS Hospital Drug Formulary. Data collection began with observation of medical records of pediatric diarrhea patients at UNS Hospital. The research data was obtained from UNS Hospital medical records for the period January - September 2023, then analyzed using the Gyssens method which was categorized as 0 - 6 descriptively and presented in the form of a percentage. This study shows the results of the rationality of antibiotics for pediatric diarrhea patients in the inpatient department of UNS Hospital using the Gyssens method for the period January - September 2023 proving that 71.73% of patients received rational antibiotic therapy (category 0), as many as 28.27% of patients received irrational antibiotic therapy including 10.87% category IVC, namely there are cheaper alternatives, 6.53% category IIIB, namely the duration of antibiotic use is too short, 10.87% category IIB, namely the interval of antibiotic administration is not appropriate.

Keywords: antibiotics; children; diarrhea; gyssens; rationality

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## INTRODUCTION

Diarrhea is a public health problem in developing countries, including Indonesia, because the morbidity and mortality rates are still high. Diarrhea is a condition in which you have loose or watery stools. Sometimes it's just water, but the frequency is more frequent (usually around 3-4 times or more per day) (Ministry of Health of the Republic of Indonesia, 2011). Diarrhea is one of the extraordinary events (KLB) that is endemic and often fatal. According to the World Health Organization (WHO) and UNICEF, there are around 2 million cases of diarrhea and 1.9 million children die from diarrhea worldwide each year. Deaths from diarrhea occur frequently in developing countries, especially in Africa and Southeast Asia (Dinkes, 2023). Based on the 2018 Riskedes report, diarrhea occurs more often in children under 5 years of age, namely 11.4% or around 47,764 cases in male patients and 10.5% or around 45,855 cases in female patients (Riskedas, 2018). According to the Health profile in Surakarta 2022, the population of diarrhea patients in the toddler category treated by medical personnel in health facilities was 1,549 toddlers or 24.63 percent of the calculation of toddler diarrhea in health facilities of 6,288 toddlers.

The low level of rationality of antibiotic use for diarrhea treatment in several hospitals, encourages researchers to evaluate the rational use of antibiotics in order to achieve therapeutic success and prevent therapeutic failure in UNS Hospital which is large with the number of diarrhea patients, especially in children. Minimizing the possible effects of antibiotic use, by using drugs rationally, it is hoped that patients will be free from adverse side effects. Irrational drug administration can result in the failure of therapy to be effective and increase the cost of treatment for patients. This study aims to examine the data on the characteristics of children with diarrhea at UNS Hospital and the percentage of rationality of antibiotic administration in children with diarrhea at UNS Hospital for the period January - September 2023 using the Gyssens method.

## **METHOD**

The following study is an observational study with a descriptive design with retrospective sampling, conducted with descriptive analysis using the Gyssens assessment method . The study was conducted to analyze the rationality of providing antibiotics for children's diarrhea at UNS Hospital for the period January - September 2023. This study has also obtained an ethical approval letter issued by the Research Ethics Committee at the Faculty of Medicine, Sebelas Maret University with the number Ethical Clearance 103 / UN27.06.11 / KEP / EC / 2024. The study was conducted at UNS Surakarta Hospital for 3 months, namely May - July 2024. Data were collected retrospectively using patient medical record data such as patient medical records and patient drug billing data . The selection of research subjects used the purposive sampling method, with the selection of research samples based on inclusion and exclusion criteria, so that the desired sample properties were obtained. Diarrhea patients aged 0 months - 9 years who were given antibiotics during hospitalization at UNS Hospital, patients who have complete medical records, patients who are not infected with other diseases, diarrhea patients in children from January - September 2023, are the inclusion criteria determined in the study. While the exclusion criteria determined in the study were patients who died during the treatment period. Gyssens method referring to the Indian Academy of Pediatrics (IAP) 2022 guidelines, Drug Information Handbook (DIH) 2006 - 2007 edition, and The Monthly Index of Medical Specialties (MIMS) 2021 edition.

Data were recorded using a data collection form that had been adjusted to the author's needs, and equipped with calculators and stationery. The samples used were documents containing patient medical records such as complete patient data, objective patient data, patient laboratory data, drug data during hospitalization, patient discharge drug data, and drug bills or patient billing during inpatient care at UNS Surakarta Hospital for the period January - September 2023. The data that was successfully collected was then analyzed using the Gyssens method which refers to the Indian Academy of Pediatrics (IAP) 2022 guidelines, the Drug Information Handbook (DIH) 2006 - 2007 edition, and The Monthly Index of Medical Specialties (MIMS) 2021 edition. The data were analyzed descriptively using a retrospective method, then transferred to a data collection sheet. The data used were obtained from the medical records of UNS Surakarta Hospital in the period January - September 2023, analyzed using the Gyssens method which was included in categories 0 - 6 descriptively and presented in percentages. Antibiotics are said to be rational if they can pass 6 categories, namely completeness of data (category VI), antibiotics are indicated (category V), more effective alternatives (category IVa), less toxic alternatives (category IVb), cheaper alternatives (category IVc), narrower alternative spectrum (category IVd), too long administration (category IIIa), too short administration (category IIIb), right dose (category IIb), right route (category IIc), right time (category I), and rational antibiotics (category 0). The results obtained after conducting the Gyssens analysis are presented in narrative and percentage form.

## RESULT

Table 1.  
Percentage data of children with diarrhea based on age at UNS Hospital

Age	f	%
0 – 11 months	5	15,16
12 -59 months	22	66.66
5 -9 years	6	18.18
Total	33	100

Most pediatric patients with diarrhea are aged 12 to 59 months with a percentage of 66.66%.

Table 2.  
Percentage of data on children with diarrhea based on gender at UNS Hospital

Gender	f	%
Man	14	42.42
Woman	19	57.57
Total	33	100

Based on table 2, the most diarrhea patients in children at UNS Surakarta Hospital were women with a percentage of 57.57%.

Table 3.  
Antibiotics used in children with diarrhea in the UNS Hospital Inpatient Installation

Types of Antibiotics	Route of Administration	Amount	Percentage (%)
Single Antimicrobial		23	69.70%
Cephalosporin group (Antibiotics)		20	60.61%
1. Cefixime po 1		3.03%	
2. Cefotaxime iv 14		42.42%	
3. Ceftriaxone iv 5		15.15 %	
Nitroimidazole Group (Antibiotics)		3	9.09%
1. Metronidazole	iv	3	9.09%
Combination antimicrobials (Antibiotics)		10	30.30%
1. Cefotaxime + metronidazole IV 4		12.12 %	
2. Ceftriaxone + metronidazole IV 2		6.06 %	
3. Cefotaxime + ceftriaxone IV 1		3.03 %	
4. Cefotaxime + ceftriaxone + metronidazole IV 3		9.09 %	

Based on table 3. it is known that the use of antibiotics in children with diarrhea at UNS Hospital is mostly a single antibiotic, namely the cephalosporin group as much as 60.6% as in other researchers, the most frequently used antibiotic group is the third generation cephalosporin (69.23%). The third generation cephalosporin group that is most frequently given is cefotaxime (42.42 % ). Drugs from the third generation cephalosporin group can penetrate tissue, body fluids, and cerebrospinal fluid, and inhibit gram-negative and gram-positive pathogenic bacteria. Cephatoxime and ceftriaxone are beta-lactam antibiotics from the third generation cephalosporin group that have a broad spectrum, with effects that can reach the central nervous system. Both can be given intramuscularly or intravenously. (Wulandari & Marintan Purba, 2017). Cefixime is used for the treatment of diarrhea with a percentage of 3.03 %. Cefixime is an antibiotic from the third generation cephalosporin group that functions to kill bacteria by inhibiting the synthesis of their cell walls. Without cell walls, bacteria will die. In addition, cefixime is a broad-spectrum antibiotic that is effective against gram-positive and gram-negative bacteria. (Wahyunita, 2017).

Table 4.  
Rationality of antibiotic prescription based on the *Gyssens method* at UNS Hospital

<i>Gyssens</i> Category	Amount of antibiotics	Patient code and antibiotic administration	Percentage (%)
Rational Category 0 (proper use of antibiotics)	33	Cefatoxime (A1, A2, A3, A4, A10, A11, A13, A14, A15, A16, A20, A21, A25, A26, A31, A32, A33)  Ceftriaxone (A9, A12, A17, A23, A28, A30)  Metronidazole (A2, A9, A11, A12, A17, A20, A26, A31, A32)  Cefixime (A19)	71.73 %
Irrational IVC Category (there are cheaper prices for antibiotics)	5	Ceftriaxone (A18, A25, A27, A31, A32)	10.87%
Category IIIB (duration of antibiotic use is too short)	3	Metronidazole (A7, A22, A29)	6.53%
Category IIB (inappropriate antibiotic administration interval)	5	Cefatoxime (A5, A6, A8, A17, A24)	10.87%
	46		100%

The administration of antibiotics for children's diarrhea must be analyzed for antibiotic rationality so as not to cause resistance, so antibiotic analysis is carried out using the *Gyssens method* which can be seen in table IV. The method of analyzing antibiotic rationality using the *Gyssens method* is to identify each antibiotic by prescribing 23 single drugs and prescribing 10 combination drugs so that the total antibiotics for which antibiotic rationality identification was carried out were 46 antibiotics.

Table 5.  
Patients who received irrational antibiotics in IVC category

Patient serial number	Antibiotics are given	Price of antibiotics given	Cheaper antibiotics	Cheaper prices for antibiotics
A18	Ceftriaxone	Rp. 37,962.00	Cefixime	Rp. 25,260.00
A25	Ceftriaxone	Rp. 37,962.00	Cefixime	Rp. 25,260.00
A27	Ceftriaxone	Rp. 37,962.00	Cefixime	Rp. 25,260.00
A31	Ceftriaxone	Rp. 37,962.00	Cefixime	Rp. 25,260.00
A32	Ceftriaxone	Rp. 37,962.00	Cefixime	Rp. 25,260.00

Table 6.  
Patients who received irrational antibiotics category IIIB

Patient serial number	Antibiotics are given	Duration of antibiotics given	Duration should be according to literature	Information
A7	Metronidazole	4 days	MIMS 2021 edition duration 5-7 days	Not Appropriate
A22	Metronidazole	3 days	MIMS 2021 edition duration 5-7 days	Not Appropriate
A29	Metronidazole	2 days	MIMS 2021 edition duration 5-7 days	Not Appropriate

Table 7.  
Patients who received irrational antibiotics category IIB

Patient serial number	Antibiotics are given	Interval of antibiotics given	The interval should be given	Information
A5	Cefotaxime	12 hours	Every 8 hours according to DIH ( <i>Drugs Information Handbook</i> )	It is not in accordance with
A6	Cefotaxome	12 hours	Every 8 hours according to DIH ( <i>Drugs Information Handbook</i> )	It is not in accordance with
A8	Cefotaxime	12 hours	Every 8 hours according to DIH ( <i>Drugs Information Handbook</i> )	It is not in accordance with
A17	Cefatoxime	12 hours	Every 8 hours according to DIH ( <i>Drugs Information Handbook</i> )	It is not in accordance with
A24	Cefotaxime	12 hours	Every 8 hours according to DIH ( <i>Drugs Information Handbook</i> )	It is not in accordance with

## DISCUSSION

Children with diarrhea due to bacterial infections are mostly under 5 years old due to the digestive tract and immune system which are still weak, resulting in pathogens that enter the body not being optimally rejected by the immune system which makes them susceptible to disease, one of which is diarrhea (Jap & Widodo, 2021). Other factors that cause diarrhea include non-exclusive breastfeeding, incomplete vaccination, inadequate hand washing methods, poor water sources, and low levels of maternal knowledge and low socio-economic status and are statistically significant factors in the occurrence of diarrhea (Nurul Fitriani, et al., 2021). The significant difference in the number of male and female diarrhea patients is because gender can affect the occurrence of diarrhea. Biological, behavioral and habitual differences can affect the incidence of diarrhea (Nurul Fitriani, et al., 2021). Women have several factors such as differences in the immune system and hormones between boys and girls. In addition, behavior and habits that involve different activities can also affect the risk of getting diarrhea (Ponirah & Harini, 2022).

In table 4 it can be seen that the results of the analysis using the Gyssens method as much as 71.73% are included in the rational category and as much as 28.27% are included in the irrational category. Irrational administration of antibiotics or inappropriate administration of antibiotics according to the pattern of infectious diseases suffered by patients is a serious

problem that can cause antibiotic resistance, prolong the disease, which is more severe can increase the risk of death, and prolong the length of stay in the Hospital. In table 5 category IVc is related to economic factors, namely the price of drugs but does not consider other costs. In this study, there were cases A18, A25, A27, A31, and A32 with a percentage of 10.86% that the price of Ceftriaxone injection at UNS Hospital was Rp. 37,962. When compared to cefixime which is a third generation cephalosporin antibiotic which is included in a similar therapeutic class. with the price of drugs at UNS Hospital is Rp. 25,260 so cefixime is cheaper than ceftriaxone. Category IIIb is related to the duration that is too short in table 6 using the standard formulary as a reference. According to the Indonesian Ministry of Health (2021) The longer the patient uses antibiotics, the more resistant bacteria will develop, because their growth is not constrained by commensal bacteria. The duration of antibiotic use according to the WHO AWaRe ( Access, Watch, Reserve ) book on the antibiotic use of ceftriaxone for 3 days and cefixime for 3 days, while according to the 2021 edition of the MIMS book on the antibiotic metronidazole the duration of use is 5-7 days and cefatoxime the duration of use is 3-5 days. In the administration of empirical therapy is 48 hours to see the response to treatment and adjust therapy if necessary. In table 6 category IIIb regarding the administration of antibiotics that are too short was found with a percentage of 6.52% in cases of patients A7, A22, and A29. The duration of antibiotic use varies, depending on the condition experienced by the patient and the severity of the disease. Category IIb in table 7 is an assessment of the accuracy of the antibiotic administration interval whether it is too often or even too rarely which will affect the excess or deficiency in the use of antibiotics. The percentage in this category is 10.86 % of these cases were obtained in cases A5, A6, A8, A17 and A24 where the accuracy of cefotaxime administration was too rare because it was given to patients every 12 hours which should have been given 4-6 hours according to the manufacturing label in the DIH ( Drugs Information Handbook ) literature for diarrhea.

In Table 4 regarding the results of antibiotic prescription rationality based on the Gyssens method at UNS Hospital from January to September 2023, 33 children with diarrhea were found. The method of antibiotic analysis using the Gyssens method is to identify each antibiotic by prescribing 23 single drugs and prescribing 10 combination drugs so that the total antibiotics given and the identification of antibiotic rationality are 46 antibiotics. Category VI regarding completeness of data and category V regarding the provision of appropriate antibiotic indications from 33 patients with a total of 46 cases are correct (0), in category IV A assessing antibiotic activity and assessed based on the outcomes achieved. The absence of category IVa is due to the antibiotics given being third-generation cephalosporins such as cefixime, cefatoxime, and ceftriaxone. These antibiotics are an alternative choice for diarrhea patients suspected of being infected with bacteria is the use of antibiotics from the cephalosporin group which function by inhibiting bacterial cell wall synthesis (Meila & Atika, 2020) while. the mechanism of action of metronidazole on bacteria is metronidazole interacts with bacterial DNA which causes damage to the DNA structure and ultimately results in bacterial cell death. and category IV B is related to the assessment of the previous category. In this assessment determines the level of drug toxicity obtained from the assessment of the suitability of the need for drugs and patient conditions. In the results of the evaluation of this category, there is no interaction of the combination of antibiotics given which has been tested using medscape. As well as the absence of toxic effects or allergic reactions to patients after administration of antibiotics during treatment at UNS Hospital.

The IVD category relates to more specific and narrow-spectrum antibiotics. The antibiotics analyzed in this study were given as empirical therapy to inhibit the growth or eliminate bacteria suspected of causing the infection, before the results of the microbiological examination were available. Therefore, the antibiotics used were broad spectrum. The selection of narrow-spectrum antibiotics must be based on the patient's blood culture results

or local bacterial patterns (Ihsan, 2021). This antibiotic therapy is a broad-spectrum antibiotic and its management is in accordance with the literature. The evaluation results did not find antibiotic absorption in diarrhea patients who were included in the IVD category. Category IIIA category with an assessment of too rapid administration of antibiotics from 33 patients with a total (46 cases) no prescription was found too fast. Category IIa is related to the accuracy of the dose which in children will be adjusted based on body surface area or conversion based on body weight. From the results obtained, no antibiotic prescription was found in children with diarrhea in category IIa due to the calculation of body weight conversion which fell into the dose calculation range. Category IIc is an assessment of the route of drug administration because in certain conditions the renewal of people is not possible such as in conditions that require immediate treatment so that the intravenous route is ideal. The evaluation results obtained in children with diarrhea are mostly through intravenous or parenteral administration because dehydration caused by diarrhea if not treated immediately will cause various harmful effects on the body and can even cause death.

The final assessment is category 1, namely timely administration. The time of administration of antibiotics to children can be seen through recording the patient's status in the medical recap and literature studies used from the results obtained by administering antibiotics to children with diarrhea at the specified time, namely 8 hours / 12 hours according to the literature. The time of administration of antibiotics is evaluated based on the time of administration each day. Timely administration of antibiotics is very important and can affect the results. A 1-hour delay can reduce survival by almost 8% (Kurniati, et al ., 2017). Category 0 regarding appropriate antibiotic prescription. Antibiotic prescription is declared appropriate if it meets the requirements such as accurate diagnosis, appropriate disease indication, correct drug selection, correct dosage, appropriate route of administration, appropriate interval of administration, appropriate duration of administration, awareness of side effects, accurate information, and appropriate assessment of the patient's condition (Ministry of Health, 2021). According to the evaluation results, antibiotic prescriptions that fall into category 0 or the rational category are 71.73% of the total number of antibiotic prescriptions for children with diarrhea who are treated at the inpatient installation of the UNS Hospital for the period January - September 2023.

## **CONCLUSION**

The rationality of antibiotics for children with diarrhea who were treated at the UNS hospital inpatient installation using the Gyssens method from January to September 2023 showed that 71.73% of patients received rational antibiotic therapy (category 0), as many as 28.27% of patients received irrational antibiotic therapy including 10.87% category IVC, namely there are cheaper alternatives, 6.53% category IIIB, namely the duration of antibiotic use is too short, 10.87% category IIB, namely the interval of antibiotic administration is not appropriate.

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