

Model prediction formulation of antibiotic type and length of treatment for pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh, Indonesia



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ABSTRACT

Introduction: Aceh Province is one of the provinces that has the highest typhoid fever cases in Indonesia and North Aceh district is also the number one highest district in Aceh province, this is certainly a special concern in dealing with the problem of appropriate antibiotic use and has effectiveness in predicting length of hospitalization. Antibiotics are drugs of the antimicrobial compound class that are generally used for bacterial infections. The use of antibiotics with good effectiveness can further shorten the length of hospitalization. This can save costs and time in the length of hospitalization, researchers want to see the effectiveness of antibiotics as a predictor of the length of treatment of pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh. This study aims to assess the effectiveness of antibiotics as a predictor of the length of treatment of pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh.

Patients and methods: The method researchers took data sources from the medical records of typhoid fever patients in children who fit the inclusion criteria, the data amounted to 160 samples and then analyzed univariate and bivariate data. All analyses considered significant if $p < 0.05$.

Results: The results showed that the characteristics of patients with typhoid fever were mostly female (63.8%) and had an age mostly in the school-age category (66.9%). The length of treatment in pediatric typhoid fever patients is mostly less than 7 days (84.4%) and the type of antibiotic used most widely used is Ceftriaxone (59.4%), more toddlers have a length of treatment of fewer than 7 days (92.3%) compared to pre-school age and school age, While school age has more length of treatment more than 7 days (18.7) than a toddler and pre-school age and female gender has more length of treatment less than 7 days (86.3%) than male, while men have more length of treatment more than 7 days (19%). Patients who used Ceftriaxone antibiotics had a longer stay of less than 7 days (87.4%) compared to other types, while patients who used Ciprofloxacin antibiotics had a longer stay of more than 7 days.

Conclusion: The type of antibiotic has a significant relationship with length of stay where Ceftriaxone antibiotics have a 2 times risk of having a length of stay of less than 7 days and age and type of antibiotic can predict the length of stay in typhoid patients.

Keywords: antibiotics, ciprofloxacin, ceftriaxone, typhoid fever.

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INTRODUCTION

Typhoid fever is a systemic infectious disease caused by *Salmonella enterica serovar typhi* (*S. typhi*) or can also be caused by *Salmonella enterica serovar paratyphi A, B, and C* which can cause infection. Typhoid fever is also known as enteric fever or is also often known by the general public as typhoid.¹

Salmonella typhi is the cause of typhoid fever. It usually enters the body through contaminated food and drink, in other

words, poor sanitation is a contributing factor. When the germ enters the body and is absorbed by the small intestine along with incoming food and drink, it will cause the germ to spread to all organs of the body, especially the liver and spleen.²

The incidence of typhoid fever in Indonesia is often found among people aged 3-19 years, who are still lacking in terms of maintaining good hygiene of themselves, the environment, food, and drinks consumed, especially at that age when immunity is still not as strong as

in adults.³ Typhoid fever is estimated by WHO to have a global burden of disease of approximately 11-20 million cases per year.⁴ In addition, typhoid fever is in the 3rd position with the most diseases in hospitalized patients. Meanwhile, the prevalence of typhoid fever cases in Indonesia reaches 350-810 per 100,000 population.⁵

The province with the highest typhoid fever cases in Indonesia was Aceh Province, which ranked first with a prevalence of 2.96% of the population. Followed by

Banten Province with a prevalence of cases as much as 2.24% of the population and in the next place is West Java Province with 2.14% of the population, the district in Aceh Province which has the highest typhoid fever cases is North Aceh District with a prevalence of 0.7% of cases and recorded in 2022 at Cut Meutia Hospital, which is one of the hospitals in North Aceh, has typhoid fever cases in children aged 0-18 years as many as 265 cases.⁶

Management that can be done in patients with typhoid fever is to do bed rest at home and self-isolation, but if it does not improve, immediately give fluids orally or parenterally so that fluids in the body remain stable and sufficient. After that, nutrition and antibiotics can be given.⁷ Antibiotics are a class of antimicrobial compounds that can suppress and stop a biochemical process in organisms, especially in infections caused by bacteria. The type of antibiotic drug for typhoid fever patients that is currently the choice is the third-generation cephalosporin class antibiotic, namely Ceftriaxone, which is proven to be more effective in fighting *Salmonella typhi* bacteria than Chloramphenicol and trimethoprim-sulfamethoxazole.⁸

The effectiveness of antibiotic use for the treatment of pediatric typhoid fever in previous studies said that fever would fall relatively faster using Ceftriaxone to shorten the length of hospitalization, and of course with lower side effects and recurrence occurring in treatment using Ceftriaxone antibiotics. This underlies the more frequent use of Ceftriaxone for the treatment of typhoid fever in hospitalized patients.⁹

From the exposure above, researchers feel interested in researching the formulation of antibiotic-type model prediction on the length of treatment of pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh. Researchers feel important because the place to be studied is also one of the districts of Aceh Province, which according to previous research data is one of the provinces and districts with the highest typhoid fever cases. It is considered important for researchers to conduct research at the Cut Meutia Hospital in North Aceh regarding the formulation of a

model prediction of antibiotic types on the length of treatment of pediatric typhoid fever patients.

METHODS

The methods in this study were taken from medical record data of pediatric typhoid fever patients who were given antibiotics at Cut Meutia Aceh Hospital.

SUBJECTS

The variable in this study is the model prediction formulation of antibiotic types on the length of treatment of pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh.

Procedure

Identification of pediatric patients with typhoid fever who were hospitalized during the specified period. Researchers will access the medical records of patients who meet the inclusion criteria. The necessary data will be collected. The collected data will be verified and validated to ensure accuracy and compatibility with the study objectives. The collected data will be organized and processed according to the planned analysis.

Locations

Cut Mutia General Hospital, North Aceh.

Data Analysis

The data analysis used in this study is univariate and bivariate analysis which is an analysis to explain and describe the effectiveness of antibiotics in predicting the length of hospitalization. This Data was then obtained from taking medical records of pediatric typhoid fever patients who were given antibiotic therapy with a total of 160 samples.

$$\text{Length of treatment} = -4.06 + 0.52 (\text{Age}) + 0.669 (\text{Types of antibiotics})$$

The Receiver Operating Characteristic (ROC) curve in this study can be seen in [Figure 1](#). The value of AUC for age is 0.583 or 58.3%, and the type of antibiotic is 0.592 or 59.2% ([Table 5](#)). Age and type of antibiotic have a value above 0.5, so it can be concluded that age and type of antibiotic can predict the length of stay in typhoid patients.

RESULTS

[Table 1](#) shows it was found that most pediatric patients were female (63.8%) and were mostly in the school-age category (66.9%). [Table 2](#) shows length of treatment in pediatric typhoid fever patients was mostly less than 7 days (84.4%) and the most widely used type of antibiotic use was Ceftriaxone (59.4%). [Table 3](#) shows that toddler age had a length of treatment of less than 7 days (92.3%) compared to pre-school age and school age, while school age had a length of treatment of more than 7 days (18.7) compared to toddlers and pre-school age. Female gender had a length of stay of less than 7 days (86.3%) compared to males, while males had a length of stay of more than 7 days (19%). In the type of antibiotic, patients who used Ceftriaxone antibiotics had a length of treatment of less than 7 days (87.4%) compared to other types, while patients who used Ciprofloxacin antibiotics had a length of treatment of more than 7 days. A bivariate test using chi-square shows that the type of antibiotic has a significant relationship with the length of treatment ($p = 0.033$).

[Table 4](#), multivariate test results show that age and type of antibiotic can predict the length of treatment in pediatric typhoid fever patients because the p -value ≤ 0.05 . The most influential variable is the type of antibiotic. This can be seen from the OR (Odds Ratio) value of antibiotic type on length of treatment is 1.95. This means that users of Ceftriaxone antibiotics have a 2 times risk of having a length of treatment of less than 7 days.

Prediction Model Formula:

$$Y = a + b_1 X_1 + b_2 X_2 + \dots + b_n X_n$$

DISCUSSION

This study looked at antibiotics as a predictor of the length of hospitalization of pediatric typhoid fever patients at the Cut Meutia Regional General Hospital in North Aceh. The patient characteristics found in pediatric typhoid fever patients at the hospital based on gender were 58

(36.3%) male patients out of 160 samples studied, and there were 102 (63.8%) female patients. This shows that the number of female patients with men is 2:1, where patients with female gender are more than men. This is supported by data from

previous research at Hasanuddin Hospital and data from the Indonesian Ministry of Health which shows that the female gender is more than male.

Then as for the characteristics of patients based on age, this research shows

several criteria. First, there are toddlers with 39 (24.4%) patients, then there is preschool age with 14 (8.8%) patients, and the most are at school age with 107 (66.9%) patients. This is also supported by the prevalence based on Indonesian Pediatric Association (IPA). Where the prevalence shows more at the age of 5 years and over called school age, IPA states that this age is vulnerable because children are familiar with food outside the home where food outside that is careless is prone to contamination with bacteria related to typhoid fever, namely *Salmonella typhi* or Paratyphi.¹⁰

Table 1. Characteristics of Gender and Age of Pediatric Typhoid Fever Patients at Cut Mutia General Hospital, North Aceh

Characteristics	Frequency (n = 161)	Percentage (100%)
Gender		
Male	58	36.3
Female	102	63.8
Age		
Toddlers	39	24.4
Pre-school	14	8.8
School-age	107	66.9

Table 2. Overview of Antibiotic Types and Length of Treatment of Pediatric Typhoid Fever Patients at Cut Mutia General Hospital, North Aceh

Characteristics	Frequency (n = 161)	Percentage (100%)
Types of antibiotics		
Ceftriaxone	95	59.4
Cefotaxime	53	33.1
Ciprofloxacin	12	7.5
Length of treatment		
≥ 7 days	25	15.6
< 7 days	135	84.4

Overview of Length of Treatment and Antibiotic Types of Pediatric Typhoid Fever Patients

The average length of treatment in pediatric typhoid fever patients at Cut Meutia Hospital North Aceh in 135 patients out of 160 samples (84.4%) had length of treatment of < 7 days and there was also an average length of treatment of more than 7 days in the remaining 25 (15.6%) patients. This can depend on the type of antibiotic used. This is in line with previous research in 2021 at Ibnu

Table 3. Relationship between gender, age, type of antibiotics, and length of treatment with antibiotic effectiveness in pediatric typhoid fever patients at Cut Mutia General Hospital, North Aceh

Variable	Length of Treatment						p
	< 7 days		≥ 7 days		Total		
	n	%	n	%	n	%	
Age							
Toddlers	36	92.3	3	7.7	39	100	0.227
Preschool	12	85.7	2	14.3	14	100	
School-age	87	81.3	20	18.7	107	100	
Gender							
Male	47	81	11	19	58	100	0.380
Female	88	86.3	14	13.7	102	100	
Types of antibiotics							
Ceftriaxone	83	87.4	12	12.6	95	100	0.033
Cefotaxime	45	84.9	8	15.1	53	100	
Ciprofloxacin	7	58.3	5	41.7	12	100	

Table 4. Prediction model of the length of treatment in pediatric typhoid fever patients at Cut Meutia General Hospital, North Aceh based on age, gender, and antibiotic type

Logistic Regression	Variable	coefficients (B)	p	OR	IK (95%)	
					min	max
Step 1	Age	0.548	0.077	1.730	0.941	3.180
	Age	0.383	0.406	0.682	0.276	1.683
	Types of antibiotics	0.633	0.047	1.883	1.008	3.517
Step 2	Age	0.523	0.050	1.687	0.923	3.084
	Types of antibiotics	0.669	0.034	1.953	1.053	3.622

Sina Hospital Makassar with the results of hospitalization time ≤ 7 days for as many as 74 patients (90.2%) and typhoid fever patients who had a hospitalization time > 7 days for as many as 8 people (9.8%). In this study the type of antibiotic that was often used was ceftriaxone because it was faster in reducing fever, the use of ceftriaxone in this study was 95 patients (59.4%). This is also in line with research at Al Islam Hospital Bandung, where ceftriaxone is the first choice drug, which has several advantages, namely low resistance to ceftriaxone in the hospital, lower side effects, fever falls faster than other types of antibiotics, which is down on day 4, as well as culture results which are the gold standard diagnosis of typhoid fever patients will produce negative results on day 4 so that the therapy time is shorter.⁹

Relationship between Age, Gender and Antibiotic Type with Length of Stay in Pediatric Typhoid Fever Patients

Research at Cut Meutia Hospital North Aceh 2022 showed that treatment of less than 7 days was dominated by toddler age with a rate of 92.3% (36 patients),

where pre-school and school age were lower. Meanwhile, school-age patients overlook, with a length of treatment of more than 7 days. Previous studies have stated that the relationship between length of hospitalization and age is not significant, but rather vulnerability at the age of 0-10 years, where at that age it is more vulnerable or often found to be hospitalized, this is because the body's immune system is still not fully formed. However, this is supported in previous research at Pertamina Bintang Amin Hospital in Lampung by Mustofa et al. where the results show that school-age children are more susceptible to salmonella typhi and paratyphi bacteria, where they are more active outside and can easily eat food and drink drinks whose hygiene is still not guaranteed.¹⁰

This study shows that the female gender has more length of treatment of less than 7 days as much as 86.3% compared to male patients, while male patients dominate the length of treatment of more than 7 days as much as 19% compared to women, but this is not yet a factor that supports that gender can affect the length of treatment. This is evidenced in previous research at

Uin Syarifhidayatullah Hospital Jakarta, where the results show that men are more dominant in typhoid fever, and men are more dominant to be more susceptible to infection and more severe in exposure, this is because men are usually more active in playing when in children and from work factors when in adults, so exposure is more susceptible to men than women. So gender cannot be a benchmark/indicator as the length of hospitalization.¹¹

The type of antibiotic also affects the length of hospitalization in this study, where ceftriaxone dominates the length of treatment of less than 7 days as much as 87.4% compared to other antibiotics, and the type of antibiotic ciprofloxacin which is a quinolone class dominates the length of treatment of more than 7 days. This is supported in the discussion above in previous studies where research at Al Islam Hospital Bandung ceftriaxone is the first choice drug because it has several advantages, namely the low resistance rate to ceftriaxone in the hospital, the side effects caused are lower, the fever drops faster than other types of antibiotics, which drops on day 4, as well as the culture results which are the gold standard diagnosis of typhoid fever patients will produce negative results on day 4 so that the therapy time is shorter. Meanwhile, the administration of ciprofloxacin is still controversial as one of the choices of antibiotic therapy for pediatric typhoid fever.⁹ This is due to its very adverse side effects which can cause arthropathy in cartilage, this causes the use of these types of antibiotics not recommended by the FDA (Food and Drug Administration) to be the choice of antibiotic therapy in the treatment of pediatric typhoid fever. The results of this study prove that ceftriaxone is more effective to be an antibiotic therapy in pediatric typhoid fever, this is supported by this study which shows a shorter length of treatment using ceftriaxone. This is also an important supporter as a prediction of the length of hospitalization where age and type of antibiotic affect the prediction, especially the type of antibiotic used, with

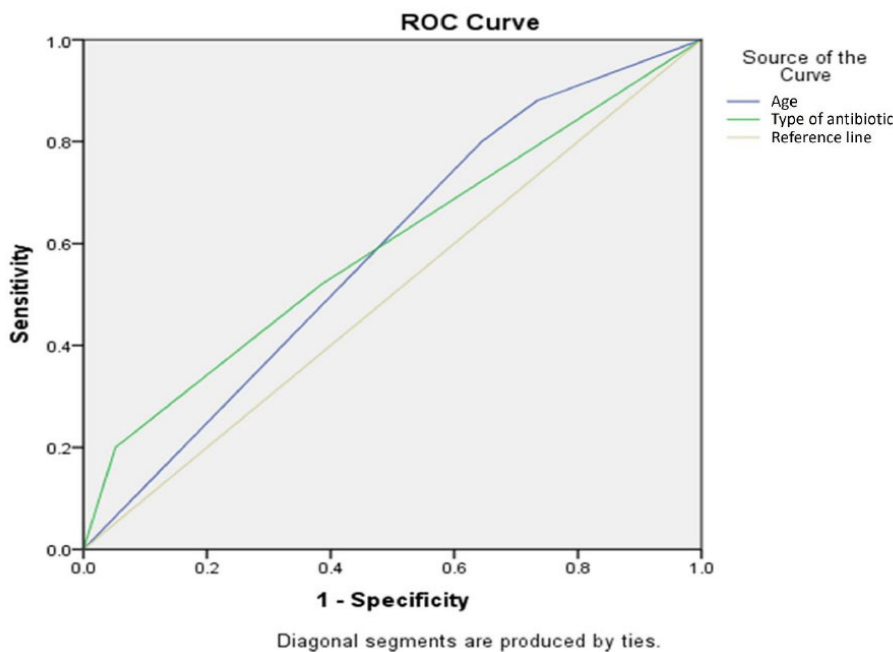


Figure 1. ROC curve of length of stay prediction by age and gender.

Table 5. AUC value for age and type of antibiotics variables

Variable	AUC (95%)	S.E	p	Cut-off	Sensitivity	Specificity
Age	0.583 (0.469-0.697)	0.058	0.187	1.5	88	73.3
Types of antibiotics	0.592 (0.462-0.772)	0.066	0.143	1.5	52	38.5

the right selection, the prediction of the length of hospitalization will be shorter.

CONCLUSION

The characteristics of patients with typhoid fever are mostly female (63.8%) and have an age mostly in the school-age category (66.9%). The length of treatment in pediatric typhoid fever patients was mostly less than 7 days (84.4%) and the most widely used type of antibiotic use was Ceftriaxone (59.4%). Toddler age was more likely to have a length of stay of less than 7 days (92.3%) compared to pre-school age and school age, while school age was more likely to have a length of stay of more than 7 days (18.7) compared to toddler and pre-school age. Female gender had a length of stay of less than 7 days (86.3%) compared to males, while males had a length of stay of more than 7 days (19%). Patients who used Ceftriaxone antibiotics had a longer stay of less than 7 days (87.4%) compared to other types, while patients who used Ciprofloxacin antibiotics had a longer stay of more than 7 days. Antibiotic type has a significant relationship with length of stay where Ceftriaxone antibiotics have a 2 times risk of having a length of stay of less than 7 days. Age and type of antibiotic can predict length of stay in typhoid patients.

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DISCLOSURE

The authors report that there are no conflicts of interest in this work.

AUTHOR CONTRIBUTION

All authors had contributed to manuscript writing and agreed for the final version of manuscript for publication.

ETHICAL CONSIDERATION

This study has been approved by The Ethical Committee of Faculty of Medicine, Universitas Malikussaleh with ethical clearance reference number 79/KEPK/FKUNIMAL-RSUCM/2023.

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