

## COST-EFFECTIVENESS ANALYSIS OF CEFTRIAXONE AND CEFIXIME IN TYPHOID FEVER PATIENTS HOSPITALIZED AT BERKAH PANDEGLANG REGIONAL HOSPITAL FOR THE PERIOD 2020-2021

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### ABSTRACT

Typhoid fever is an infectious disease among humans caused by the bacterium *Salmonella typhi*. With the high Multi-Drug Resistance (MDR) of *Salmonella typhi*, selecting the right antibiotic is a factor that must be considered in addition to cost constraints. Therefore, cost-effectiveness is needed. This study aims to determine the cost-effectiveness of typhoid fever patients using ceftriaxone and cefixime antibiotics. The data used are retrospective, and the sampling was done by purposive sampling. This study was conducted at Berkah Pandeglang Regional Hospital. Sample in this study, namely typhoid fever patients of the period 2020-2021, who meet the inclusion and exclusion criteria. In this study, 16 samples were obtained. The results of this study showed that the total average direct medical costs for the ceftriaxone group were IDR 78.632.500. In contrast, the cefixime group was IDR 75.527.300. The ACER value of typhoid fever patients who used Ceftriaxone + cefixime was IDR 91,646.27, Ceftriaxone was IDR 77,463.89, and cefixime was IDR 88,027.15. The patients with typhoid fever who used Ceftriaxone were more cost-effective than those who used Cefixime.

**Keywords:** Typhoid Fever; Ceftriaxone; Cefixime; Cost-Effectiveness Analysis

## 1. INTRODUCTION

In Indonesia, infectious diseases are considered a health problem that humans often face. One condition that can transmit is disease that can transmit it is typhoid fever. Typhoid fever is a disease that can infect fellow humans, caused by the occurrence of a *Salmonella typhi* bacteria. These bacteria infect the digestive tract, resulting in an inflammatory process in the small intestine and intestinal lumen (Agnes et al., 2019). Typhoid fever is one type of infection that cannot be taken lightly. The incidence of typhoid fever varies in each region and is usually related to environmental sanitation (Gunawan et al., 2020). The treatment of typhoid fever is constantly evolving. This disease requires therapy capable of dealing with *Salmonella typhi* infection. The therapy used for typhoid fever includes symptomatic and antibiotic therapy. The first-line antibiotics used to treat typhoid fever are chloramphenicol, penicillin and trimethoprim/sulfamethoxazole (Yunita et al., 2018). Chloramphenicol is one of the drugs of choice in treating typhoid fever. However, along with advances in medicine, developed drugs such as sulfonamides, cephalosporins, and fluoroquinolones (Pratiwi et al., 2018).

Typhoid fever patients given third-generation cephalosporin group antibiotics such as Ceftriaxone are typhoid fever patients who experience antibiotic resistance to other typhoid fever drugs (Hidayah et al., 2020). Ceftriaxone is an antibiotic that has been considered potent and effective for treating typhoid fever because it can selectively damage the structure of germ cells and does not interfere with other body cells (Jannah et al., 2019). According to research conducted

by Yusransyah et al., (2023) the used of antibiotics Ceftriaxone costs IDR 33,028,179 and Cefixime costs IDR 170.861.998 in road care patients.

A disease that requires a good pharmacoeconomic assessment. The drug's effectiveness and its economic value is typhoid fever. Typhoid fever is a systemic disease that is characterized by fever and abdominal pain and arises as a result of infection with *Salmonella typhi* and *Salmonella Paratyphi* (Magfirah, 2019). Improper use of antibiotics with indications of the patient's disease will have a bad impact, resulting in longer patient therapy treatment, so the treatment cost becomes expensive (Purwanti et al., 2014). Costs directly related to health services patients bear during hospital stays include the cost of patient hospitalization per night, examination costs, medical procedure costs, doctor's fees, and administrative costs (Aulia et al., 2017). The cost required to organize and utilize public health services is a health cost. Its main purpose is to maintain and improve health and prevent typhoid fever (Khoirin & Arismunandar, 2021). To achieve the cost-effectiveness of typhoid fever, therapy can use health economic analysis, that is cost-effectiveness analysis, called cost-effectiveness analysis (CEA), which means economic evaluation methods that can be used for decision-making in choosing an alternative drug that is best for the treatment (Tuloli, 2017).

The pharmacoeconomic analysis is a comprehensive method that aims to determine the existence of an alternative economic effect of drug therapy or intervention on other health (Yusransyah et al., 2023). Pharmaceutical intervention is used to assess whether or not there is an additional cost of a benefit to the intervention that is commensurate with the previously added cost of the previous intervention (Jannah et al., 2017). National Health Insurance (BPJS) annual financial report records showed deficits of IDR 3.8 trillion in 2014, IDR 5.9 trillion (2015), IDR 9.7 trillion (2016), IDR 10 trillion (2017), and an estimated IDR 16.2 trillion in 2018 respectively. Another study also stated that in the cost-effectiveness analysis of typhoid fever treatment at Dr M.M. Dunda Limboto Hospital in 2017, the cost of treatment for ceftriaxone antibiotic therapy was IDR 3,650,091 with a length of hospitalization of 2.8 days compared to the cefotaxime antibiotic therapy group with a greater cost of IDR 4.036.015 with a length of stay of 3.7 days (Tuloli, 2017).

Berkah Pandeglang Regional Hospital is a regional hospital that is a treatment centre in Pandeglang Regency and City. Previously, no research related to pharmacoeconomics at the Berkah Pandeglang Regional Hospital had been conducted on typhoid fever. Therefore, research related to pharmacoeconomics is needed, one of which is the analysis of cost-effectiveness in typhoid disease to provide appropriate drug therapy services and the costs incurred are small so that there is no loss for workers at Berkah Pandeglang Regional Hospital or for patients which is a form of quality control and cost control. Based on the background, this study aims to determine the cost-effectiveness of therapy between Ceftriaxone and cefixime in typhoid fever patients admitted to the Berkah Pandeglang Regional Hospital for the period 2020-2021.

## 2. METHODS

### 2.1. Research Design

This type of research uses the non-experimental method of data retrieval retrospectively using secondary data. Secondary data is already available in the hospital in medical records and medical expenses of typhoid fever patients at Berkah Pandeglang Regional Hospital.

### 2.2. Data Collection Methods

Sampling in this study uses a non-probability method with a purposive sampling technique. Purposive sampling is a sampling technique that is based on the characteristics that have been determined by researchers (Ahyar et al., 2020). The data collected includes medical record data and cost data. Medical record data includes the patient's name, medical record number, age,

gender, antibiotic therapy used, and length of hospitalization days. Cost Data includes the cost of drugs, laboratories, medical procedures, hospitalization, doctor visits, and medical devices.

Secondary patient Data that can be used as a sample in this study must meet the inclusion and exclusion criteria. The inclusion criteria in this study, namely BPJS patients, gender, diagnosed with typhoid fever without comorbidities, hospitalized at Berkah Pandeglang Regional Hospital in the period 2020-2021, given ceftriaxone or cefixime antibiotics during treatment at the hospital, and declared cured of typhoid fever by a doctor. Exclusion criteria in this study, namely typhoid fever patients with incomplete medical record data, missing and not clearly readable, patients with forced discharge or death, and experienced a change of antibiotics during hospital treatment.

### 2.3. Data Analysis

Data analysis of this study using the calculation of the value of ACER (Average Cost Effectiveness Ratio). Data obtained from medical records and cost data are processed and stored using the Microsoft Excel number program. Data processing in the Microsoft Excel Numbers program aims to determine each group's average total cost and effectiveness value. Then, the average total cost and effectiveness values are entered into the ACER formula. ACER calculation results show that therapy is cost-effective. Therapy is said to be cost-effective if the therapy has the smallest ACER value compared to other therapies. Acer formula follow Eq. 1.

$$ACER : \frac{\text{Average Total Cost}}{\text{Effectiveness}} \quad (1)$$

Statistical test in this study aims to determine the difference in meaning between research variables. Statistical tests were used: Mann-Whitney for cost data and independent sample t-test for effectiveness data.

## 3. RESULTS AND DISCUSSION

This research was conducted at Berkah Pandeglang Regional Hospital and was carried out starting in February-June 2022. Data collection is done by purposive sampling. The data taken is in the form of medical record data and cost data of typhoid fever patients who are hospitalized in RSUD Berkah Pandeglang. Based on the inclusion and exclusion criteria, a sample of 20 patients was obtained. The samples were then classified based on antibiotics that are often used in patients during hospital treatment.

The samples in this study were divided into ceftriaxone and cefixime antibiotics. Patients taking Ceftriaxone + cefixime were 9 patients, and Ceftriaxone was 4 patients. Patients taking Ceftriaxone + cefixime were 9 patients, and cefixime was 3 patients. As well as patients who only use Ceftriaxone, there are 4 patients, and cefixime, there are 3 patients. Typhoid fever patients are treated in the room (Class 2, Class 3), and the main room with payment of all hospital treatment costs borne by the BPJS (Payer). The data obtained will be processed based on the characteristics of patients and will be analyzed pharmaco-economically with the method of Cost-Effectiveness Analysis (CEA) to obtain the most cost-effective intervention group.

### 3.1. Patient Characteristics

Gender characteristics in typhoid fever patients hospitalized in Berkah Pandeglang Regional Hospital period 2020-2021 can be seen in [Table 1](#). Characteristics of typhoid fever patients hospitalized at Berkah Pandeglang Regional Hospital period 2020 - 2021. Female patients are more numerous than male patients. Male typhoid fever patients amounted to 6 (47%), while female typhoid fever patients amounted to 10 (63%). This Data is in accordance with the data in a study conducted by Alfen (2018), which shows that the number of typhoid fever patients with female sex is more compared to male sex patients ([Hidayat, 2018](#)). In the spread of typhoid fever,

there is no difference between men and women who will have a risk for typhoid fever (Rangki & Fitriyani, 2019). However, typhoid fever is more common in men, with a percentage of 58.53%. Men have higher activity than women (Puspasari et al., 2020). Unlike most cases where typhoid fever is often found in the male type because there are differences in activity between the male and female groups. This difference is possible because in this study the majority of respondents based on the medical records of the Hospital are women. However, it does not exclude the possibility that male typhoid fever sufferers also have high incidence rates (Mustofa et al., 2020).

**Table 1.** Characteristics By Gender of The Patient

Gender	Total of Patients	Percentage (%)
Male	6	47
Female	10	63
Total	16	100

The age characteristics of typhoid fever patients hospitalized at Berkah Pandeglang Regional Hospital for 2020-2021 can be seen in Table 2. The age characteristics of typhoid fever patients who were hospitalized at the Berkah Pandeglang Regional Hospital for the period 2020-2021 showed that the highest age group was the age of 42-58 years after that followed by patients aged 18-25 years and 33-37 years. Typhoid fever is closely related to the quality of the profound views of the hygiene factors in the environment, such as individual hygiene and hygiene in public places, such as restaurants and restaurants, and public behavior that does not support a healthy lifestyle (Jannah et al., 2017). Based on Table 2 at the age of adulthood, a person's activity outside the home is high, causing exposure to *Salmonella typhi* to increase.

**Table 2.** Characteristics By Age of The Patient

Age (Years)	Total of Patients	Percentage (%)
18-25	4	25
26-37	4	25
38-58	8	50
Total	16	100

Table 3 show the characteristics of antibiotic therapy that is often used in typhoid fever patients hospitalized at the Berkah Pandeglang Regional Hospital for the period 2020-2021, in Ceftriaxone + cefixime as many as 9 patients (56%), Ceftriaxone as many as 4 patients (25%) and cefixime as many as 3 patients (19%). When viewed from both antibiotics, ceftriaxone antibiotics are the most commonly used antibiotics because there is a high antibacterial potential with a broad spectrum and low potential for toxicity. It is widely used that Ceftriaxone is a class of third-generation cephalosporin antibiotics where the antibiotic is an antibiotic that has a broad spectrum that can cope with both gram-negative and gram-positive bacteria (Jannah et al., 2017).

**Table 3.** Characteristics Based on Antibiotic Therapy

Antibiotic Therapy	Total of Patients	Percentage (%)
Ceftriaxone + Cefixime	9	56
Ceftriaxone	4	25
Cefixime	3	19
Total	16	100

### 3.2. Cost of Treatment Analysis

This study uses the perspective of the payer, IE. All costs will be borne by the company concerned (institutions) such as BPJS. Therefore, the appropriate cost component for the analysis of the study is direct medical costs.

The study results are shown in **Table 4**. The highest average total cost is found in the group of patients who use Ceftriaxone with a total cost of IDR 78.632.500 and an average of IDR 6,048,654. While in the group of patients who use cefixime has a total cost of IDR 75.527.300 with an average cost of IDR 5.809.792. The SPSS Mann Whitney test analysis showed significant  $p = 0.01 < 0.05$ , so it can be concluded that there is a significant difference between the cost of typhoid fever patients who use Ceftriaxone and cefixime.

The drug cost is the cost that each patient must pay during treatment for the entire drug used, such as antibiotics, vitamins, and others. The cost of the drug is influenced by the type and amount of the drug used, the duration of treatment, and the symptoms that the patient is experiencing. The average cost of drugs in this study amounted to IDR 490.000 in the group of patients given Ceftriaxone and IDR 378,000 in the group of patients given Cefixime.

**Table 4.** Treatment Cost Data

Average Cost	Antibiotic	
	Ceftriaxone	Cefixime
Drugs	IDR 490.000	IDR 378.000
Laboratory	IDR 15.229.000	IDR 14.809.000
Medical Measures	IDR 32.329.500	IDR 31.121.800
Hospitalization	IDR 12.800.000	IDR 12.100.000
Doctor Visit	IDR 1.948.000	IDR 1.873.000
Medical Devices	IDR 15.836.000	IDR 15.345.500
Total Medical Direct	IDR 78.632.500	IDR 75.527.300
Average	IDR 6.048.654 (13 patients)	IDR 5.809.792 (12 patients)
ρ-Value	0,001	

### 3.3. Duration of Hospitalization

Duration of hospitalization is a description of the duration or length of a patient who is hospitalized in a health facility. The duration of hospitalization can be affected by the severity of the disease, the side effects of the drug, and the possibility that the patient has taken the drug before admission to the hospital.

The results of the study are shown in **Table 5**. patients with long hospitalizations using Ceftriaxone + cefixime were 9 patients (66%), patients with long hospitalizations using Ceftriaxone were 4 patients (75%), and patients with long hospitalizations using cefixime were 3 patients (66%). The Independent Sample Analysis Test T-Test showed the significance of  $p = 0.690 > 0.05$ . Because  $> 0.05$ , it can be ascertained that there is no significant difference between the length of hospitalization of typhoid fever patients who use Ceftriaxone + cefixime with Ceftriaxone.

**Table 5.** Assessment of Length of Stay

Antibiotic Therapy	Total patient		Effectiveness	p-Value
	length of stay (<5 days)	Total of all patients		
Ceftriaxone + Cefixime	6	9	66	0.690
Ceftriaxone	3	4	75	
Cefixime	2	3	66	

### 3.4. Cost-Effectiveness Analysis

Cost-Effectiveness Analysis (CEA) is used to select and assess the best health or treatment program from several treatment options with the same treatment goals. Cost Effectiveness



Analysis converts cost and effectiveness through the ratios (Khoiriyah & Lestari, 2018). The goal is to see which strategy costs less per unit of output or gives the most output for a given number of available costs (Indrayathi, P.A & Noviyanti, 2016). ACER values obtained in this study can be seen in Table 6.

In this study, cost-effectiveness was seen by comparing the cost incurred with the treatment outcome between the ceftriaxone and cefixime groups. The cost of ACER compares the average direct medical costs with the effectiveness of each drug (Yusransyah et al., 2022). The results from ACER are interpreted as the average cost per unit of effectiveness. The smaller the ACER value, the more cost-effective the alternative drug. So it can be concluded that antibiotics with the lowest cost are the most cost-effective (Khoiriyah & Lestari, 2018). The effects in this study were measured from the average length of hospitalization of each therapy group. Ceftriaxone is more cost-effective than cefixime (Lorensia et al., 2018).

Typhoid fever patients are given Ceftriaxone more cost-effectively than those given Ceftriaxone + cefixime. Typhoid fever patients with cefixime are more cost-effective than those with Ceftriaxone + cefixime. Patients with typhoid fever who were only given Ceftriaxone were more cost-effective than patients given Cefixime. Therefore, in this study, the most cost-effectiveness is the ceftriaxone group. This result is not by the study of Jannah et al., (2017) which explains that the ACER value obtained by patients using Ceftriaxone IDR 61.796,06 is greater than typhoid fever patients who use Cefixime IDR 60.781,97. This is because there is a difference in terms of the length of hospitalization in these patients. The lower the value of ACER, the more cost-effective because the use of low drug costs is able to provide higher results of use (Jannah et al., 2017).

**Table 6.** ACER value

Antibiotic Therapy	Average direct medical costs	Effectiveness (%)	ACER
Ceftriaxone + Cefixime	IDR 6.048.654	66	IDR 91,646.27
Ceftriaxone	IDR 5.809.792	75	IDR 77,463.89
Cefixime	IDR 5.809.792	66	IDR 88,027.15

#### 4. CONCLUSION

This study concludes that the group of typhoid fever patients who use Ceftriaxone is more cost-effective compared to the group of typhoid fever patients who use Cefixime. The government and or hospitals can reconsider using cefixime drugs in typhoid fever patients and may make Ceftriaxone an option in managing typhoid fever patients.

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