

Research Article

Comparative Analysis of Cost Effectiveness of Ceftriaxone and Cefotaxime Antibiotic Therapy in Inpatients with Typhoid Fever in Aulia Pandeglang Regional Hospital in 2023

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ABSTRACT

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Typhoid fever is still a significant health problem for children in developing countries, including Indonesia. This disease is caused by infection with *Salmonella Typhi* bacteria, which is a Gram-negative bacteria and requires treatment with antibiotics. The use of antibiotics usually takes up a large portion of the hospital treatment budget. This study aims to compare the cost-effectiveness between two types of antibiotics, namely ceftriaxone and cefotaxime, in typhoid fever patients at Aulia Pandeglang Hospital, and to find the most cost-efficient treatment. This study is descriptive and observational, with retrospective data collection. The data used came from medical records and cost records of inpatients with typhoid fever in children aged 1 to 11 years at Aulia Pandeglang Hospital in 2023. A total of 20 patients met the study criteria. The outcomes measured in this study were the average length of stay in the hospital. The cost components calculated consisted of direct medical costs, such as drug costs, action costs, inpatient costs, medical device costs, and laboratory fees. The analysis was conducted from the payer's perspective. The results showed that the cost for the effectiveness of using ceftriaxone and cefotaxime was IDR 15,264 and IDR 18,265, with an ICER of IDR 257.9 to increase the effectiveness of cefotaxime. The conclusion of this study is that ceftriaxone is a more cost-effective antibiotic.

Keywords: typhoid fever; cost effectiveness; ceftriaxone; cefotaxime

INTRODUCTION

Infectious diseases are still a major challenge in public health in Indonesia. One of these infectious diseases is typhoid fever. Typhoid fever is caused by infection with the *Salmonella typhi* bacteria which attacks the digestive tract and causes inflammation of the small intestine and intestinal lumen. This disease can be transmitted between humans and can attack anyone, both children and adults (Agnes, Citraningtyas, and Sudewi 2019).

Typhoid fever is a serious infectious disease and should not be taken lightly. The incidence of typhoid fever varies from region to region and is often influenced by environmental sanitation conditions. In Indonesia, the disease is still endemic, with an estimated 800 out of every 100,000 people contracting typhoid fever each year and cases can be found almost all year round (Andayani and Fibriana 2018).

Typhoid fever cases are often found in children and adolescents aged between 3 and 19 years. The age group of 5 to 11 years, which is school age, tends to be more susceptible to infection because they often do activities outside the home. Children in this group have immune systems that are not as strong as adults and often do not maintain cleanliness when eating or drinking and do not always wash their hands properly after urinating or defecating (Musthofa 2021).

Antibiotics are the main therapy for treating typhoid fever. However, in order to maximize its effectiveness and to prevent side effects and resistance, the use of antibiotics must be carried out appropriately and rationally. The appropriate use of antibiotics not only affects the effectiveness of treatment but also has an impact on cost efficiency by increasing therapeutic effects (Idrus et al. 2023). On the other hand, inappropriate use of antibiotics can cause various problems, such as suboptimal healing, increased risk of side effects, higher treatment costs, and the emergence of resistance (Zuhdi et al. 2024).

The high rate of Multi Drug Resistance (MDR) in *Salmonella typhi* makes the selection of alternative antibiotics an important factor that needs to be considered, in addition to cost issues. To achieve therapeutic effectiveness in the treatment of typhoid fever, cost-effectiveness analysis can be used. Cost-effectiveness analysis is an economic evaluation method that helps in decision-making to choose the most optimal treatment alternative (Adisasmito 2016).

Pharmacoeconomic analysis is a more comprehensive method, which aims to assess the economic impact of alternative drug therapies or interventions on other aspects of health (Akhyani et al. 2024). In pharmaceutical interventions, pharmacoeconomics is used to evaluate whether the benefits obtained from the intervention are worth the additional costs incurred, compared to the previous intervention (Jannah, Ihwan, and Tandah 2019).

Several pharmacoeconomic evaluations have been conducted in the field of infectious diseases to guide optimal resource utilization. For example, a study by Marasine et al. (2021) in Nepal assessed the cost-effectiveness of different antibiotic regimens in sepsis management and found that timely administration of the right antibiotics significantly reduced hospital costs and mortality (Marasine et al. 2021). Similarly, Mas-Dalmau et al. (2023) demonstrated that pharmacoeconomic evaluations in respiratory infections can identify treatments that provide better health outcomes at lower costs (Mas-Dalmau et al. 2023). In typhoid fever specifically, evaluations comparing oral and injectable antibiotic regimens have shown that pharmacoeconomic insights are essential for formulating hospital treatment guidelines and minimizing unnecessary expenditures (Saito, Parry, and Yeung 2018; Ujjan et al. 2024). These studies highlight the growing role of pharmacoeconomic research in infectious disease management, especially in settings with limited healthcare budgets.

In cost-effectiveness studies of antibiotic treatment for typhoid fever, clinical outcomes such as duration of fever recovery, length of hospital stay, and complete recovery without complications are often used as indicators of effectiveness (Musnelina, Tanama, and Teodhora 2024). Therefore, this study will use the number of patients who recovered (clinical perfection) and the average length of hospital stay as the primary outcomes to assess the effectiveness of ceftriaxone and cefotaxime treatment.

Several previous studies have conducted pharmacoeconomic evaluations in the context of typhoid fever treatment. For example, a study by Yusransyah et al. (2023) in Pandeglang compared ceftriaxone and cefixime and found that ceftriaxone therapy was more cost-effective than cefixime (Yusransyah et al. 2023). Similarly, a study conducted by Pinem et al. (2021) evaluated the cost-effectiveness of various antibiotic regimens in Medan and highlighted that ceftriaxone is more cost-effective than levofloxacin (Pinem et al. 2021). This study emphasizes the relevance and application of pharmacoeconomic analysis in selecting rational and sustainable treatment options for typhoid fever.

This study aims to compare the cost-effectiveness between two types of antibiotics, namely ceftriaxone and cefotaxime, in typhoid fever patients at Aulia Pandeglang Hospital, and to find the most cost-efficient treatment. The results of this study are expected to provide evidence-based recommendations that can support hospital formularies, local clinical guidelines, and health financing decisions in resource-limited settings. By identifying the more cost-effective antibiotic between ceftriaxone and cefotaxime, this research will help policymakers optimize healthcare resource allocation while maintaining treatment efficacy and patient safety. This is particularly relevant for Indonesia's national

health insurance system (JKN), which requires sustainable and efficient use of medicines in clinical practice (Mahendradhata et al. 2017).

MATERIALS AND METHODS

The type of research conducted is non-experimental research that is observational, with direct medical cost calculations obtained from patient medical records. The data collection method is carried out retrospectively using secondary data.

The population in this study were all pediatric patients who were confirmed to have typhoid fever and were hospitalized at Aulia Pandeglang Hospital. The sample of this study included pediatric patients who met certain criteria. The sample criteria in this study were patients aged 1-11 years who were diagnosed with typhoid fever without comorbidities, patients with complete medical records and cost data, and patients who received ceftriaxone or cefotaxime antibiotic treatment during treatment at Aulia Pandeglang Hospital.

The sampling technique used is purposive sampling. Data collection was carried out using patient medical records and direct medical cost data obtained from the medical record installation and financing installation at Aulia Pandeglang Hospital.

Data analysis in this study was conducted descriptively, with the aim of describing the characteristics of each variable and evaluating the cost-effectiveness between ceftriaxone and cefotaxime therapy in typhoid fever patients at Aulia Hospital.

The outcome measured in this study was the average length of hospitalization (in days). The difference in effectiveness between the ceftriaxone and cefotaxime groups was statistically analyzed using the independent t-test to determine the results of length of hospitalization and cost outcomes, with the level of significance set at $p < 0.05$.

Cost analysis in this study was conducted from the payer's perspective. Cost data were obtained from hospital billing records and included only direct medical costs. Cost components included in the analysis are drug costs, action costs, inpatient costs, medical device costs, and laboratory fees. All costs are calculated in Rupiah (IDR) using actual hospital costs per patient as recorded in the financial system.

To measure the cost-effectiveness of the two antibiotic therapies, both Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) were calculated. ACER was calculated by dividing the total cost by the number of effective outcomes (i.e., recovered patients) for each antibiotic

group. ICER was calculated by comparing the difference in cost and the difference in effectiveness between cefotaxime and ceftriaxone groups.

RESULTS

Characteristics of Typhoid Fever Patients

Based on the data obtained, patients were grouped according to several characteristics, such as age, gender, and length of hospitalization. The results of data collection from typhoid fever patients who were hospitalized at Aulia Hospital, Pandeglang Regency, during the period January-December 2023 showed that there were 20 patients who met the criteria for this study. The sample of this study was divided into two groups, namely the group receiving treatment with ceftriaxone and the group receiving cefotaxime, with each group consisting of 10 patients.

Table 1. Characteristics of Typhoid Patients

Characteristics	N = 20	
	Frequency(n)	Percentage (%)
Sex		
a. Male	7	35%
b. Female	13	65%
Age		
a. 1-7 Years	15	75%
b. 8-11 Years	5	25%
Length of Stay		
a. 1 Day	3	15%
b. 2 Days	2	10%
c. 3 Days	6	30%
d. 4 Days	4	20%
e. 5 Days	3	15%
f. 6 Days	2	10%

Gender distribution showed that female patients were more dominant (65%) than male patients (35%). Most patients (75%) were in the age range of 1-7 years, while the rest (25%) were aged 8-11 years. The length of hospitalization of patients varied, with the highest percentage (30%) being treated for 3 days, followed by 4 days (20%), 1 day and 5 days (each 15%), and 2 days and 6 days (each 10%) (Table 1). These demographic characteristics are important for understanding the population studied and may affect the interpretation of cost-effectiveness results. Differences in the proportion of sex and age may reflect disease patterns or differences in access to health services, while variations in length of hospitalization may be an indicator of disease severity or response to therapy given.

Cost Calculation

This study adopts a payer perspective using direct medical cost data. The types of direct medical services generally included in the inpatient cost data for typhoid fever patients in this study include drug costs, action costs, inpatient costs, medical device costs, and laboratory fees.

Table 2. Cost Data for Children with Typhoid Fever Patients

Type of Fee	Ceftriaxone	Cefotaxime
Drug Costs	IDR 276,700	IDR 257,020.8
Action Costs	IDR 369,200	IDR 325,600
Inpatient Costs	IDR 380,300	IDR 464,000
Medical Device Costs	IDR 87,800	IDR 72,950
Laboratory Fees	IDR 107,150	IDR 99,000
Total	IDR 1,221,150	IDR 1,218,571
p-Value	0.173	

The data in Table 2 shows that the average total direct medical costs of pediatric typhoid fever patients using ceftriaxone therapy at Aulia Pandeglang Hospital were IDR 1,218,571. These results indicate that the average total cost in the ceftriaxone group was slightly higher than in the cefotaxime group. The results of the statistical test showed a p-value of 0.173 (>0.05), so it can be interpreted that there is no significant difference in costs between the two groups. In this study, the type of cost that had the highest average value compared to other direct medical costs was the cost of hospitalization, while the type of cost that had the lowest average value was the cost of medical equipment.

Effectiveness of Treatment Therapy

Based on research by Hidayah et al. (2020), it was found that typhoid fever patients who were hospitalized for 5 days did not show optimal effectiveness. Based on the discussion above, in this study, a sample can be declared valid if the Length of Stay (LoS) or treatment time value is less than 5 days.

The primary clinical outcome measured in this study was the duration of hospitalization as an indicator of clinical recovery, with effectiveness defined as discharge in less than 5 days. This was selected as a practical and observable marker of patient improvement. The inclusion criteria ensured that all patients had no comorbidities or complications, as verified through physician records and clinical assessments.

Table 3. Analysis of Treatment Effectiveness

Group	Effectiveness				Total	%
	<5 day	%	>5 day	%		
Ceftriaxone	8	80%	2	20%	10	100
Cefotaxime	7	70%	3	30%	10	100
p-Value	0.043					

Based on Table 3, the results of this study indicate that Ceftriaxone has a higher effectiveness, with 80% of patients recovering in less than 5 days, compared to Cefotaxime which has a cure rate of 70%. This 10% difference indicates that Ceftriaxone may be more effective in accelerating the recovery of pediatric typhoid fever patients compared to Cefotaxime. To assess whether the difference in effectiveness was statistically significant, an independent sample t-test was performed. The results showed that the difference was not statistically significant with a p-value of 0.043 ($p > 0.05$), indicating a comparison of effectiveness between the two antibiotic therapies. Treatment effectiveness is an important factor in cost-effectiveness analysis because it directly affects patient health outcomes and total treatment costs incurred.

Cost-Effectiveness Analysis

Cost-effectiveness analysis (CEA) is a relatively simple pharmacoeconomic technique often used to compare two or more health interventions with different effect sizes. Using CEA, we can determine the most cost-effective form of health intervention while still considering its effectiveness in achieving the desired outcome, such as patient recovery or improved quality of life. This analysis helps policymakers and health care providers choose the optimal treatment option in terms of costs and benefits (Kementrian Kesehatan RI 2013).

Table 4. ACER calculation

Therapy Group	Total cost	Effectiveness (%)	ACER (total cost/effectiveness)
Ceftriaxone	IDR 1,221,150	80	IDR 15,264
Cefotaxime	IDR 1,218,571	70	IDR 18,265

Table 4 shows that the ACER (Average Cost-Effectiveness Ratio) value for Ceftriaxone is IDR 15,264, while the ACER value for Cefotaxime is IDR 18,265. A lower ACER value indicates better cost-effectiveness. In this context, Ceftriaxone has a lower ACER, which means that for each unit of effectiveness achieved, the cost incurred is lower compared to Cefotaxime. In other words, Ceftriaxone is more efficient in producing one unit of effectiveness (cure in less than 5 days) compared to Cefotaxime.

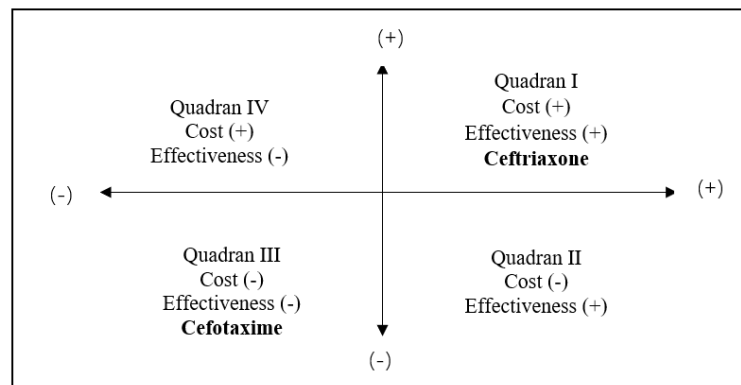


Figure 1. Cost Effectiveness Quadrant

Ceftriaxone therapy has a higher total cost and effectiveness, so it is in Quadrant I, while Cefotaxime therapy has a lower total cost and effectiveness, so it is in Quadrant III. Based on the results of this cost-effectiveness quadrant analysis, additional considerations need to be made in calculating the ICER (Incremental Cost-Effectiveness Ratio). ICER will help to determine the extent to which the increase in the effectiveness of therapy (such as faster recovery) is comparable to the increase in costs incurred. In other words, ICER can provide a clearer picture of whether the higher-cost therapy (Ceftriaxone) actually provides comparable added value compared to the cheaper therapy (Cefotaxime) (Kementrian Kesehatan RI 2013).

Table 5. ICER calculation

Intervention	Cost	Effectiveness	ICER Value
Ceftriaxone- Cefotaxime	IDR 2,579	10%	IDR 257.9

ICER (Incremental Cost-Effectiveness Ratio) calculation is needed to determine the additional cost required to achieve increased efficacy in pediatric typhoid fever patients. Based on the results in Table 5, it was found that an additional cost of IDR 257.9 was required to increase efficacy in the Ceftriaxone treatment group compared to Cefotaxime. This means that for every unit increase in efficacy (e.g., faster recovery in less than 5 days), an additional cost of IDR 257.9 was required when using Ceftriaxone compared to Cefotaxime. Cost-effectiveness indicators such as ACER and ICER were calculated using the observed difference in clinical response (i.e., length of hospitalization <5 days), although the difference was not statistically significant.

DISCUSSION

Based on the gender characteristics in Table 1, it can be seen that most of the typhoid fever patients treated at Aulia Pandeglang Regional Hospital between January and December 2023 were female. This study is consistent with the findings of Yusransyah et al. (2024), which also showed that typhoid fever sufferers were more common among women (Yusransyah et al. 2024). The distribution of sufferers based on gender tends to be higher in women than men, which is likely influenced by various factors such as poor personal hygiene, poor food and drink hygiene, and an unhygienic environment, all of which can contribute to the incidence of typhoid fever.

The results of the study based on age characteristics showed that the most cases of typhoid fever in 2023 occurred in patients aged 1 to 7 years at the inpatient facility of Aulia Pandeglang Hospital. This finding is in line with the research of Pratiwi et al. (2022), which showed that patients aged 1 to 7 years tend to pay less attention to personal hygiene compared to patients aged 8 to 14 years. Children in this age range are more active and often pay less attention to diet and hygiene, which increases the risk of contracting typhoid fever. The highest incidence occurs in school-age children, who are greatly influenced by hygiene factors. The bacteria that cause typhoid, *Salmonella typhi*, mainly grow in unhygienic food (Nuraini, Garna, and Respati 2015).

Based on the characteristics of the hospitalization period for typhoid fever patients, it can be concluded that the most common hospitalization period for patients is 3 days. This study is in line with the findings of Pratiwi et al. (2022), which stated that the most cases were typhoid fever patients with a hospitalization period of 3 days, as many as 48 patients. This is due to the use of Ceftriaxone or Cefotaxime antibiotic therapy in pediatric typhoid patients. Fever symptoms usually subside on the 4th day, and culture results become negative on the same day, after which the patient can be discharged (Pratiwi & Putri, 2022).

Overall, the total costs for both treatment groups were similar, with Ceftriaxone slightly more expensive (IDR 1,221,150) compared to Cefotaxime (IDR 1,218,571). However, there were differences in cost components. Drug and procedure costs were higher in the Ceftriaxone group, while hospitalization costs were higher in the Cefotaxime group. Costs for medical devices and laboratories were relatively similar between the two groups. These differences in cost structure may be due to differences in drug prices, treatment protocols used, and length of hospitalization that may be influenced by patient clinical factors. These cost differences are important to consider in the context of hospital resources and patient ability to pay. Similar studies in developing countries have also

highlighted the importance of cost analysis in antibiotic selection, especially with increasing antimicrobial resistance (Otioku et al. 2024).

Treatment effectiveness measured by the proportion of patients who recovered in less than 5 days showed that Ceftriaxone had better effectiveness (80%) compared to Cefotaxime (70%). This finding is in line with several studies that show the superiority of Ceftriaxone in accelerating symptom resolution and shortening hospitalization in typhoid fever patients (Bhandari et al. 2024). This difference in effectiveness is due to the more favorable pharmacokinetics and pharmacodynamics of Ceftriaxone, such as better tissue penetration and stronger bactericidal activity against *Salmonella typhi* (Sharma et al. 2024).

Cefotaxime is given at a dose of 1 g by intramuscular injection and has been shown to be almost 100% effective, both from a clinical and microbiological perspective. Meanwhile, Ceftriaxone is considered a potent and effective drug for the short-term treatment of typhoid fever. The advantages of this drug include its selective ability to damage the structure of microorganisms without harming human body cells, its broad spectrum of action, and relatively low microbial resistance (Jannah, Ihwan, and Tandah 2019).

Based on Table 4, the ACER calculation results show that the Ceftriaxone group spent IDR 15,264, while the Cefotaxime group spent IDR 18,265. In pediatric typhoid fever patients hospitalized at Aulia Pandeglang Hospital, it was found that the Ceftriaxone therapy group was more cost-effective than Cefotaxime therapy based on the efficacy parameter of length of hospitalization. This study is consistent with the findings of Jannah et al. (2019), who found that Ceftriaxone therapy was more effective than Cefotaxime, with an ACER value of IDR 346,357 per case per day.

Based on the cost-effectiveness quadrant analysis, Ceftriaxone is located in Quadrant I, which shows higher costs and effectiveness compared to Cefotaxime. In contrast, Cefotaxime is located in Quadrant III, which shows lower costs and effectiveness. These results provide an overview of the relative position of the two therapies in terms of cost and effectiveness. Although Ceftriaxone is more expensive, its higher effectiveness makes it more efficient in producing better health outcomes, which then encourages further analysis using ICER to evaluate the additional costs required to achieve increased effectiveness.

The ICER value in this study was IDR 257.9, which means that for every 10% increase in effectiveness using Ceftriaxone compared to Cefotaxime, there is an increase in costs of IDR 2,579. This ICER value shows the trade-off between additional costs and additional benefits of using Ceftriaxone. Interpretation of the ICER value should consider the willingness-to-pay threshold that is relevant to the

local context. If the ICER value is below this threshold, Ceftriaxone can be considered a cost-efficient option.

In Indonesia, the commonly used cost-effectiveness threshold based on WHO-CHOICE guidelines is one to three times the GDP per capita per quality-adjusted life year (QALY) gained, which in 2023 is estimated to be between IDR 62 million and IDR 186 million per QALY (Marseille et al. 2015; World Bank 2023). Although our study does not express effectiveness in QALYs, the ICER value of IDR 257.9 per 10% improvement in recovery is substantially lower than the lowest WTP threshold. This suggests that Ceftriaxone remains a highly cost-effective intervention within the Indonesian healthcare context.

The findings of this study have important implications for clinical practice and health policy. In the context of limited resources, cost-effectiveness analysis can help hospitals make informed decisions about resource allocation for typhoid fever treatment. Although this study provides valuable evidence, there are several limitations. The relatively small sample size and observational study design limit the generalizability of the findings. Further studies with prospective designs and larger sample sizes are needed to confirm these results and explore other factors that influence the cost-effectiveness of typhoid fever treatment.

Future studies are recommended to use larger sample sizes and multi-center settings to improve the generalizability of findings. It is also important to include prospective designs with longer follow-up to assess not only short-term recovery but also relapse rates and potential long-term complications. In addition, future research should incorporate sensitivity analysis and budget impact analysis to support decision-making at the institutional and policy levels. Evaluating patient-reported outcomes and health-related quality of life could also provide a more comprehensive assessment of cost-effectiveness in pediatric typhoid fever treatment.

CONCLUSIONS

Based on the results and discussion, this study concluded that Ceftriaxone showed better treatment effectiveness than Cefotaxime in treating typhoid fever in children at Aulia Pandeglang Hospital. This is evidenced by the proportion of patients who recovered in less than 5 days, which was higher in the Ceftriaxone group (80%) compared to the Cefotaxime group (70%). Although the total cost of treatment between the two groups did not differ significantly, the cost-effectiveness analysis using ACER showed that Ceftriaxone was more efficient in terms of cost per unit of effectiveness.

ICER analysis indicates that increased effectiveness with Ceftriaxone requires additional costs that need to be considered in the context of the hospital's

willingness to pay threshold. Overall, considering the higher effectiveness and cost efficiency, Ceftriaxone may be a more profitable option in the treatment of typhoid fever in children at Aulia Pandeglang Hospital. However, the final decision must still consider the individual clinical factors of the patient and the availability of hospital resources.

This study has some limitations, including the relatively small sample size, retrospective design, and absence of sensitivity analysis. These factors may limit the generalizability and robustness of the findings.

Given the minimal cost difference and favorable ICER values, switching from Cefotaxime to Ceftriaxone may be beneficial, especially in situations where faster recovery and shorter hospital stays are priorities. However, the decision should be aligned with institutional antibiotic stewardship policies and drug availability.

ETHICAL ISSUES

This research has passed the research ethics review from the Health Research Ethics Committee (Non-Medical) of Prof. Dr. Hamka Muhammadiyah University with letter number 03/24.03/03185.

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