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# ANALYSIS OF COST EFFECTIVENESS OF ANTIBIOTIC USE IN TYPHOID FEVER PATIENTS AT KARTINI RANGKASBITUNG HOSPITAL IN 2022

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**ABSTRAK**

Penyakit demam tifoid merupakan salah satu penyakit yang memiliki angka prevalensi yang tinggi sehingga menjadi permasalahan kesehatan di Indonesia. Satu-satunya golongan obat yang menjadi alternatif untuk mengatasi penyebab utama demam tifoid, yaitu antibiotik. Antibiotik menjadi salah satu jenis terapi obat yang membutuhkan banyak anggaran untuk pengadaannya. Tujuan dari penelitian ini, yaitu untuk mengetahui jenis antibiotik yang paling *cost-effective* untuk mengatasi demam tifoid. Rumah Sakit Kartini Rangkasbitung menjadi lokasi penelitian secara observasional dengan pendekatan potong-lintang. Penelitian ini menggunakan data retrospektif dengan jenis data yaitu data sekunder. Data rekam medis dan data biaya menjadi sumber data pada penelitian ini. Pada penelitian ini terbagi menjadi tiga kelompok, yaitu ciprofloxacin tablet, seftriaxone intravena, levofloxacin tablet dan levofloxacin intravena. Berdasarkan hasil perhitungan didapatkan nilai ACER dari ceftriaxone adalah IDR 2.955.250, nilai ACER levofloxacin IV adalah IDR 2.727.306, dan nilai ACER dari levofloxacin tablet adalah IDR 3.047.337. Nilai ICER yang dihasilkan dari perbandingan antara Levofloxacin tablet dengan Ceftriaxone, yaitu IDR 43.250. Antibiotik yang paling *cost-effective* adalah antibiotik Levofloxacin dalam bentuk Intravena.

Kata Kunci: **Demam Tifoid, Terapi Antibiotik, Efektivitas Biaya**

**ABSTRACT**

*The high prevalence rate of typhoid fever is one of the health problems in Indonesia. Antibiotic therapy is the only therapy that can be used to treat the main cause of typhoid fever. Antibiotics are a type of drug therapy that requires a lot of budgets to procure. This study aims to find out the most cost-effective type of antibiotic for treating typhoid fever. This research was conducted at Kartini Rangkasbitung Hospital using observational research methods with a cross-sectional approach. The data used uses secondary data conducted retrospectively. This research uses medical record data and cost data. This study was divided into three groups, namely ciprofloxacin tablets, intravenous ceftriaxone, levofloxacin tablets and intravenous levofloxacin. Based on the calculation results, the ACER value of ceftriaxone is IDR 2,955,250, the ACER value of IV*

*levofloxacin is IDR 2,727,306, and the ACER value of levofloxacin tablets is IDR 3,047,337. The ICER value from the comparison between levofloxacin tablets and ceftriaxone is IDR 43,250. The most cost-effective antibiotic is the antibiotic levofloxacin in intravenous form.*
*Keywords:* ***Typhoid Fever, Antibiotic Therapy, Cost-Effectiveness***

## 1. INTRODUCTION

According to the World Health Organization (WHO), the number of cases and deaths due to typhoid fever reaches 600,000, with 17 million cases reported each year. According to UN data, the Asian continent accounts for 70% of cases (Kementerian Kesehatan Republik Indonesia, 2013; World Health Organization, 2016). The World Health Organization (WHO) reported that in 2018, the number of typhoid fever cases in Indonesia reached 11-12 million cases per year, causing the deaths of between 128,000 and 161,000 people each year. Currently, the number of typhoid fever cases in Indonesia has reached 55,098 cases, which is a death rate of 2.06% of the number of sufferers. The spread of typhoid fever is the tenth ranked disease in Indonesia (Kementerian Kesehatan RI, 2020).

Antibiotic therapy in typhoid fever patients uses various types of antibiotics, including chloramphenicol, ampicillin, amoxicillin, sulfonamides, fluoroquinolones, and cephalosporins (Lestari & Karyus, 2020). However, according to reports from several countries, chloramphenicol, ampicillin, amoxicillin, sulfonamides have Multi Drug Resistance (MDR) problems in Salmonella typhi so they will not be examined in this study. Cases of multidrug-resistant Salmonella typhi are associated with disease progression, similar to the risk of toxicity, hypertension, and even death (Andrews et al., 2018).

The quinolones, such as ciprofloxacin and levofloxacin, third generation cephalosporins, such as ceftriaxone and ceftazidime, and azithromycin are some of the third-generation cephalosporin antibiotics that are often used as substitutes for chloramphenicol. Ceftriaxone is a third generation cephalosporin that has high stability against gram-negative bacteria, making it effective against bacteria that cause typhoid fever (Andrews et al., 2018). Third-generation cephalosporins are also effective in stopping bacterial growth and overcoming resistance to chloramphenicol, ampicillin, amoxicillin, and sulfonamides, as shown by in vitro studies (Andrews et al., 2018). It is known that fluoroquinolone antibiotics reduce fever very well, and microbiological test results show that they have no significant side effects (Akram et al., 2020; World Health Organization, 2019).

The choice of antibiotics that is not in accordance with the disease indication will cause the patient's treatment to take longer and the cost of treatment will be more expensive. During a hospital stay,

patients must pay for medication use, hospitalization, laboratories, and medical procedures (Aulia, 2017).

To make health services more efficient and economical, pharmacoeconomic analysis is needed, because the WHO statement shows that the cost of antibiotic treatment for typhoid fever patients is relatively high and cannot guarantee that the treatment is effective (Hazimah, Priastomo, & Rusli, 2019). Pharmacoeconomics is used in pharmacy to determine the results of treatment in proportion to the costs incurred by patients to receive treatment (Yusransyah, Rahmawati, Udin, & Kurnia, 2023).

According to research by Tuloli, (2017), ceftriaxone antibiotic therapy in typhoid fever patients at Dr. Regional Hospital. M. M. Dunda Limboto average cost IDR 3,650,091 with a length of stay of 2.8 days, cheaper than cefotaxime, which costs IDR 4,036,015 with a length of stay of 3.7 days. These results contradict the research of Oktafiani, (2017), who found that the antibiotic cefotaxime was cheaper than ceftriaxone at Ambarawa Regional Hospital. This is where pharmacoeconomic research on cost-effectiveness is very important. Cost-effectiveness analysis is used to compare the use of alternative medicines for certain diseases to find cheaper medicines.

The antibiotics used to treat typhoid fever vary. Each type of antibiotic used will produce different effectiveness. In addition, the use of a type of antibiotic can affect the cost of treatment. Therefore, a pharmacoeconomic study such as a cost-effectiveness analysis is needed to find therapies that have high effectiveness at low costs. The aim of this study, based on the description above, is to determine which antibiotic is the most cost-effective to use in typhoid fever patients at the Kartini Rangkasbitung Hospital Inpatient Installation.

## 2. RESEARCH METHODS

### 2.1 Research Design

This research is a cross-sectional observational study with an analytical nature. Data collection was carried out through the process of tracing patient data in medical records and the costs of treating typhoid fever treated at Kartini Rangkasbitung Hospital, Lebak Regency in 2022.

### 2.2 Population and Sample

This research uses medical records and cost data for inpatients with typhoid fever at Kartini Rangkasbitung Hospital as a population. The sample in this study was medical records and cost data for typhoid fever patients who met the inclusion and exclusion criteria at Kartini Rangkasbitung Hospital. The number of samples in this study was 84 patients.

### 2.3 Inclusion and Exclusion Criteria

The inclusion criteria for this study were medical records of typhoid fever patients treated at Kartini Rangkasbitung Hospital during 2022, typhoid fever patients who were given single antibiotic therapy, patients who were allowed to go home by the doctor because they recovered, and complete and legible medical record data. Meanwhile, the exclusion criteria in this study were typhoid fever patients who were forced to return home or died, typhoid fever patients

with comorbidities, typhoid fever patients with combination antibiotic therapy, typhoid fever patients who during hospitalization experienced a transition to the use of antibiotic therapy.

### 2.4 Data Analysis

The Microsoft Excel number processing program was used for data processing in this research. After the data has been collected, the data is entered into Microsoft Excel software and processed using the ICER and ACER formulas. The ACER and ICER values are the final values which are the basic form of assessing the cost-effectiveness of the antibiotic therapy being compared. The ICER value is carried out if each therapy is not located in a dominant position in the cost-effectiveness table.

$$\textbf{Formula ACER} = \frac{\text{Total Direct Medical Costs (IDR)}}{\text{Clinical Outcomes (\%effectiveness)}}$$

$$\textbf{Formula ICER} = \frac{\text{Cost A} - \text{Cost B}}{\text{effectiveness A} - \text{effectiveness B}}$$

## 3. RESULTS AND DISCUSSION

Data was collected from Kartini Rangkasbitung Hospital, located in Lebak Regency, Banten. The sampling method used was the total sampling technique. Data from medical records of typhoid fever patients who were hospitalized at Kartini Hospital from January to December 2022 were used in this study. Based on the antibiotics used, samples were classified into Levofloxacin, Ciprofloxacin, and Ceftriaxone.

Patient characteristics such as gender, antibiotic therapy, payment status, length of stay, and direct costs of treatment and drugs can be determined from research results using pharmacoeconomic cost-effectiveness analysis. The data collected is used to determine the most effective antibiotic treatment.

In pharmacoeconomic studies, Cost-Effectiveness Analysis (CEA) is used to compare two or more health interventions that have different effect sizes. CEA can also be used to select health interventions that provide the greatest value for limited funds (Setiawan, Endarti, & Suwantika, 2017).

**Table 1.** Characteristics of Typhoid Fever Patients

| No | Characteristics | N | % |
|---|---|---|---|
| 1 | **Sex** | | |
| | Male | 39 | 46 |
| | Female | 45 | 54 |
| | **Total** | **84** | **100** |
| 2 | **Age** | | |
| | <5 Years | 6 | 7 |
| | 5-11 Years | 31 | 37 |
| | 12-16 Years | 16 | 19 |
| | 17-25 Years | 15 | 18 |
| | 26-35 Years | 12 | 14 |
| | 36-45 Years | 4 | 5 |
| | **Total** | **84** | **100** |
| 3 | **Payment status** | | |
| | General | 16 | 19 |
| | BPJS | 65 | 77 |
| | Private insurance | 3 | 4 |
| | **Total** | **84** | **100** |
| 4 | **Antibiotic therapy used** | | |
| | Levofloxacin (Intravena) | 51 | 60,7 |
| | Levofloxacin (tablet) | 21 | 25,0 |
| | Ceftriaxone (Intravena) | 9 | 10,7 |
| | Ciprofloxacin (Tablet) | 3 | 3,6 |
| | **Total** | **84** | **100** |

**Table 1** shows that the number of typhoid fever patients treated in the inpatient ward at Kartini Rangkasbitung Hospital from January to December 2022 is more female than male. This research is in accordance with research by Nadyah, (2014), where the majority of respondents were female (37.74 percent), while the fewest were male (13.26 percent). In this study, female had a much greater risk than male. However, Pramitasari's research, (2013) found that male are more susceptible to typhoid fever compared to female, because men do more activities outside the home, so they prefer to eat fast food or food stalls which usually contain flavorings that are not guaranteed. and unhygienic. Female prefer to eat at home rather than outside the home, so female is not susceptible to typhoid fever. This habit makes men more susceptible to diseases transmitted through food, such as typhoid fever. A study conducted by the Ministry of the Republic of Indonesia found that female are more likely to get typhoid fever than male (Pramitasari, 2013).

**Table 1** shows that typhoid fever patients treated at Kartini Rangkasbitung Hospital consisted of 31 patients (37%) aged 5-11 years which was the group with the highest number of samples and aged 36-45 years was the group with the lowest number of samples, 4 patients. (5%). Every individual can get typhoid fever. Children aged five to fifteen years old are in school and often do activities outside the home. This could lead to the risk of being infected with Salomonella typhi due to snacks at school or unclean food and drinks. Children can be more easily contaminated with Salmonella typhi due to hygiene factors, body resistance, and contamination of milk or milk products by

carriers (Kementerian Kesehatan Republik Indonesia, 2013).

Based on **Table 1**, the BPJS payment status is the most widely used of all payment statuses, with a total of 65 patients. The purpose of presenting this data is to show how many patients use national health insurance (JKN). This data was collected from inpatients with typhoid fever at Kartini Hospital. It is hoped that the results of this study will be useful for insurance providers when selecting antibiotics for typhoid fever patients treated under assisted status because more and more patients are using assisted status.

The types of antibiotics used to treat typhoid fever are levofloxacin (iv), levofloxacin (tablets), ceftriaxone (iv), and ciprofloxacin (tablets). Based on data collected from Kartini Hospital, Lebak Regency, levofloxacin (iv) was used most frequently with a total of 51 patients used in this study. The fluoroquinolone class of antibiotics includes levofloxacin. The mechanism of action of this antibiotic consists of stopping bacterial topoisomerase II or DNA gyrase and topoisomerase IV. Termination of topoisomerase II is required during transcription and replication, and termination of topoisomerase IV prevents replicated DNA chromosomes from separating from each other during cell division. In one day, the general oral and intravenous dose is 500-750 mg. Side effects of levofloxacin include nausea, headache, diarrhea, and insomnia (Yunita, Pramestutie, Illahi, & Achmad, 2018).

**Table 2.** Comparison of Therapy Effectiveness

| Antibiotic Therapy | Effective | | Ineffective | |
|---|---|---|---|---|
| | n | % | n | % |
| Ciprofloxacin Tablet | 0 | 0 | 3 | 100 |
| Ceftriaxone IV | 6 | 66,7 | 3 | 33,3 |
| Levofloxacin Tablet | 15 | 71,4 | 6 | 28,6 |
| Levofloxacin IV | 36 | 70,5 | 15 | 29,5 |

Differences in the effectiveness of antibiotic therapy results are based on differences in length of stay. The length of treatment time can be used as a measure of the performance of a hospital's health services. The length of patient care can assess the efficiency of a health service. Antibiotics are said to be effective if the patient is hospitalized for no more than 5 days (Kementerian Kesehatan Republik Indonesia, 2006). In this study, the results of antibiotic therapy were said to be effective if the patient who used antibiotic therapy was hospitalized for no more than five days. The percentage of effectiveness is obtained from the number of patients hospitalized for no more than five days divided by the total number of patients and multiplied by 100% (Laode, Nasruddin, Surdam, Nurelly, & Syahril, 2021). The highest percentage of effectiveness was in patients using Levofloxacin i.v. antibiotic therapy. namely 70.5% (36 patients out of a total of 51 patients). The results of Ciprofloxacin therapy showed a figure of 0% because there were only 3 patients and

all of them were treated for more than 5 days so they did not meet the minimum threshold for the effectiveness of antibiotic therapy based on inpatient parameters. Data on the effectiveness of antibiotic therapy will be used to calculate the ACER value for each therapy.

**Table 3.** Data on Direct Medical Costs

| Antibiotic Therapy | Medical Procedure Costs (IDR) | Laboratory Fees (IDR) | Pharmacy Costs (IDR) | Total Cost (IDR) |
|---|---|---|---|---|
| Ciprofloxacin Tablet | 1.137.050 | 393.382 | 581.521 | 2.111.953 |
| Ceftriaxone IV | 747.546 | 583.000 | 637.651 | 1.968.197 |
| Levofloxacin Tablet | 1.131.758 | 409.190 | 634.851 | 2.175.799 |
| Levofloxacin IV | 895.866 | 338.216 | 688.669 | 1.922.751 |

The type of costs analyzed for CEA are direct medical costs, which in this case consist of costs for medical procedures and rooms, laboratory examination costs and costs for antibiotics and drugs used for accompanying symptoms. Based on data obtained from inpatients with typhoid fever who were treated at Kartini Rangkasbitung Hospital, direct treatment data for inpatients was obtained which included costs for hospitalization and medical procedures, laboratory examination costs, and pharmacy billing costs. Based on the data above, the highest direct medical costs are medical costs for patients using levofloxacin tablets, namely IDR 2,175,799. The lowest total costs for patients using levofloxacin infusion antibiotic therapy are IDR 1,922,751. Cost-effectiveness analysis was carried out using the Average cost-effectiveness ratio (ACER) calculation method. ACER describes the total cost of an alternative program or therapy divided by clinical outcomes to provide an illustration of the cost ratio in currency units per specific clinical outcome obtained. Direct treatment cost data obtained from typhoid fever patients at Kartini Hospital was then used to calculate the cost-effectiveness ratio expressed by ACER (Average cost effectiveness ratio). Calculating this ratio, the results will show alternative antibiotic therapy that has the lowest direct medical costs per outcome obtained (direct medical costs/day).

**Table 4.** Cost Effectiveness Analysis

| Antibiotic therapy | Total Direct Medical Costs (IDR) | Effectiveness (%) | ACER value |
|---|---|---|---|
| Ciprofloxacin Tablet | 2.111.953 | 0% | - |
| Ceftriaxone IV | 1.968.197 | 66,6% | 2.955.250 |
| Levofloxacin Tablet | 2.175.799 | 71,4% | 3.047.337 |
| Levofloxacin IV | 1.922.751 | 70,5% | 2.727.306 |

The ACER value or average cost-effectiveness ratio of a choice of several alternative therapies that have the same goal is the ratio with the lowest value. Based on the ACER calculation results shown in table 4, it can be seen that the lowest ACER value is the average cost-effectiveness ratio of Levofloxacin i.v. antibiotic therapy namely 2,727,306. Alternative therapy options that are more

cost-effective are alternative therapies with a lower ACER value than others (Kementerian Kesehatan RI, 2013). This shows that Levofloxacin i.v. is an antibiotic therapy option that is more cost-effective compared to other antibiotic options used for inpatients with typhoid fever at Kartini Rangkasbitung Hospital.

To strengthen the ACER calculation results that have been obtained, a cost-effectiveness comparison between antibiotic therapies will be carried out. This comparison is mapped in a comparison table of antibiotics based on cost-effectiveness. This mapping will reveal which antibiotics are the main choice based on the high and low cost-effectiveness obtained compared to other antibiotics.

**Table 5.** Cost Effectiveness

| Cost-Effectiveness | Lower costs | Same cost | Higher costs |
|---|---|---|---|
| Lower effectiveness | A<br>Ceftriaxone<br>Levofloxacin IV | B | C<br>Ceftriaxone |
| Same effectiveness | D | E | F |
| Higher effectiveness | G<br>Levofloxacin IV | H | I<br>Levofloxacin Tablet |

In this study, 3 comparisons of the cost effectiveness of antibiotic therapy were carried out based on the cost effectiveness table, namely comparisons between IV Levofloxacin and Levofloxacin tablets, IV Levofloxacin with Ceftriaxone and Ceftriaxone with Levofloxacin tablets. Based on the comparison between Levofloxacin IV and Levofloxacin tablets, the position of Levofloxacin IV is in column A and the Levofloxacin tablet is in column I. This shows that the comparison between Levofloxacin IV and Levofloxacin tablets can be calculated by ICER.

Based on the comparison between IV Levofloxacin and Ceftriaxone, the position of IV Levofloxacin is in column G and Ceftriaxone is in column C. This shows that antibiotic therapy using IV levofloxacin is more recommended as the choice of antibiotic therapy for typhoid fever patients in the Kartini Rangkasbitung Hospital ward, so ICER does not need to be taken into account. Based on the comparison of Ceftriaxone with Levofloxacin tablets, Ceftriaxone is in column A and Levofloxacin tablets are in column I. This shows that the comparison of Ceftriaxone with Levofloxacin tablets can be continued in the ICER calculation. Based on the grouping results in the cost-effectiveness table, it shows that the comparison of antibiotic therapy that can be continued in the ICER calculation, namely the comparison between Levofloxacin tablets and Ceftriaxone and the comparison between Levofloxacin tablets and Levofloxacin IV.

**Table 6.** ICER Calculation Results

| Antibiotics | Δ Cost (IDR) | Δ Effectiveness (%) | ICER (IDR) |
|---|---|---|---|
| Levofloxacin Tablet-Ceftriaxone | 207.602 | 4,8 | 43.250 |
| Levofloxacin Tablet – Levofloxacin IV | 253.048 | 0,9 | 281.164 |

The table above shows the ICER values from the comparison of levofloxacin tablets with ceftriaxone and levofloxacin tablets with IV levofloxacin. The ICER value shows that if the patient wants to increase the effectiveness of therapy, it is necessary to add a cost of IDR 43,250 per increase in one unit of effectiveness to the comparison of levofloxacin tablets with ceftriaxone, while in the comparison of levofloxacin tablets with levofloxacin IV, that is IDR 281,164 per increase in one unit of effectiveness. The ICER value resulting from this comparison is in accordance with the ICER calculation formula in Kementrian Kesehatan RI, (2013) regarding pharmacoeconomic guidelines. Based on the resulting ICER value, the additional costs that must be incurred by IV ceftriaxone and levofloxacin users in order to obtain equivalent effectiveness to levofloxacin tablets are very large so that it will increase the cost burden for patients and insurance providers, therefore, in a cost-effectiveness comparison, it is more recommended using antibiotic therapy which has a higher cost (difference IDR207,602/IDR253,048) but has higher effectiveness, namely levofloxacin tablet antibiotic therapy.

## 4. CONCLUSION

The conclusion of this study is that the ACER value of ceftriaxone is IDR 2,955,250, the ACER value of IV levofloxacin is IDR 2,727,306, and the ACER value of levofloxacin tablets is IDR 3,047,337. The ICER value of the comparison between Levofloxacin tablets and Ceftriaxone is 43,250, while the comparison between Levofloxacin tablets and Levofloxacin IV has an ICER value, namely IDR 281,164. The most cost-effective antibiotic is the one with the lowest ACER value, namely the antibiotic Levofloxacin in IV form.

## BIBLIOGRAPHY

Akram, J., Khan, A. S., Khan, H. A., Gilani, S. A., Akram, S. J., Ahmad, F. J., & Mehboob, R. (2020). Extensively Drug-Resistant (XDR) Typhoid: Evolution, Prevention, and Its Management. *BioMed Research International*, *2020*. https://doi.org/10.1155/2020/6432580

Andrews, J. R., M.D., F., Qamar, N., F.C.P.S., R., Charles, C., & Edward T. Ryan, M. D. (2018). Extensively Drug-Resistant Typhoid — Are Conjugate Vaccines Arriving Just in Time? *New England Journal of Medicine*, *379*(16), 1491–1493. https://doi.org/10.1056/nejmp1805927

Aulia. (2017). *Evaluasi Penggunaan Antibiotik Pada Pasien Pneumonia Di Rumah PKU Muhammadiyah Bantul*. Universitas Muhammadiyah Yogyakarta.

Hazimah, K. W., Priastomo, M., & Rusli, R. (2019). Analisis Efektivitas Biaya Penggunaan Antibiotik pada Pasien Demam Tifoid di RS SMC Periode 2017. *Jurnal Sains Dan Kesehatan*, *2*(2), 107–114. https://doi.org/10.25026/jsk.v2i2.126

Kementerian Kesehatan Republik Indonesia. (2006). *Keputusan Menteri Kesehatan RI Nomor 364/MENKES/SK/V/2006 tentang Pedoman Pengendalian Demam Tifoid*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan Republik Indonesia. (2013). *Sistematika Pedoman Pengendalian Penyakit Demam Tifoid*. Jakarta: Direktorat Jendral Pengendalian Penyakit & Penyehatan Lingkungan.

Kementrian Kesehatan RI. (2013). *Pedoman Penerapan Kajian Farmakoekonomi*. Jakarta: Kementerian Kesehatan RI.

Kementrian Kesehatan RI. (2020). *Pedoman Pengendalian Demam Tifoid*. Jakarta: Kementrian Kesehatan Republik Indonesia.

Laode, M. I. S. P., Nasruddin, H., Surdam, Z., Nurelly, & Syahril, E. (2021). Karakteristik pasien demam tifoid di Rumah Sakit Ibnu Sina Makassar. *Wal'afiat Hospital Journal*, *02*(02), 141–148.

Lestari, D. J. T., & Karyus, A. (2020). Penatalaksanaan Demam Tifoid pada Lansia dengan Pendekatan Kedokteran Keluarga. *Jurnal Kedokteran*, *9*(1), 40–48.

Nadyah. (2014). Hubungan faktor-faktor yang mempengaruhi insidens penyakit demam tifoid di kelurahan samata kecamatan somba opu kabupaten gowa 2013. *Jurnal Kesehatan*, *VII*(1).

Oktafiani, E. (2017). *Analisis Efektivitas Biaya Penggunaan Injeksi Seftriakson Dan Sefotaksim Pada Pasien Demam Tifoid Di Instalasi Rawat Inap RSUD Ambarawa Tahun 2016*. Universitas Setia Budi Surakarta.

Pramitasari, O. P. (2013). Faktor Risiko Kejadian Penyakit Demam Tifoid Pada Penderita Yang Dirawat Di Rumah Sakit Umum Daerah Ungaran Okky. *Jurnal Kesehatan Masyarakat 2013*, *2*(1), 1–10. Retrieved from http://ejournals1.undip.ac.id/index.php/jkm

Setiawan, D., Endarti, D., & Suwantika, A. (2017). *Buku Farmakoekonomi Modeling*. Purwokerto: UM Purwokerto press.

Tuloli, T. S. (2017). Cost-Effectiveness Analysis Terapi Antibiotik Seftriakson dan Sefotaksim Pada Pasien Tifoid di RSUD Dr. M.M Dunda Limboto. *Jurnal Entropi*, *12*(1), 97–103. Retrieved from https://media.neliti.com/media/publications/277411-cost-effectiveness-analysis-terapi-antib-6014239e.pdf

World Health Organization. (2016). Focus of Tifoid Fever, Weekly.

World Health Organization. (2019). Table of Contents Essential Medicine List Application for Special Indication : Typhoid and Paratyphoid Fever.

Yunita, W. C., Pramestutie, H. R., Illahi, R. K., & Achmad, A. (2018). Analisis Cost-Minimization Penggunaan Sefotaksim, Seftriakson dan Levofloksasin pada Pasien Demam Tifoid dengan Status Pembayaran Umum dan Jaminan Kesehatan Nasional : Penelitian dilaksanakan di Rumah Sakit Daerah Kanjuruhan Kepanjen. *Pharmaceutical Journal of Indonesia*, *4*(1), 11–15.

Yusransyah, Y., Rahmawati, Y., Udin, B., & Kurnia, N. M. (2023). Cost-Effectiveness Analysis of Ceftriaxone and Cefixime in Typhoid Fever Patients Hospitalized At Berkah Pandeglang Regional Hospital for the Period 2020-2021. *Jurnal Farmasi Sains Dan Praktis*, *9*(2), 178–184. https://doi.org/10.31603/pharmacy.v9i2.8648