Cost-Consequence Analysis of Levofloxacin Compared to Ceftriaxone in Community-Acquired Pneumonia of Adult Inpatients at X Hospital Surakarta

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Abstract

Background: *Community-acquired pneumonia is still a significant cost-burden disease in healthcare facilities. Pharmacoeconomic analysis using the cost-consequence analysis (CCA) method of ceftriaxone compared to levofloxacin as a first-line empirical antibiotic has never been carried out.* **Objective**: *to model the clinical and economic impact of administering ceftriaxone as a first-line empirical antibiotic compared to its comparator levofloxacin for community-acquired pneumonia therapy in hospitalized adult inpatients from the perspective of healthcare facilities.* **Methods**: *This research is a retrospective observational study that collects medical records and patient billing data in X Hospital Surakarta from January to December 2022 period. The study was conducted from June to July 2023. Subjects were adult inpatients aged ⩾ 18 years with community-acquired pneumonia and were given levofloxacin or ceftriaxone as first-line empiric antibiotics. The data taken included patient profile, antibiotic effectiveness and direct medical costs. Cost-consequence analysis (CCA) was used to compare levofloxacin to ceftriaxone to assess their impact on length of stay, antibiotic effectiveness, and direct medical costs based on a healthcare perspective.* **Results**: *The antibiotic effectiveness for levofloxacin was 75.00%, and ceftriaxone was 93.33%. The average length of stay for levofloxacin was 3.39 days, and ceftriaxone was 3.00 days. The total direct medical costs for levofloxacin were IDR 2,056,799, and ceftriaxone was IDR 1,969,627.* **Conclusion**: *The administration of ceftriaxone to levofloxacin as a first-line empirical antibiotic for community-acquired pneumonia in hospitalized adult patients had the consequence of increasing antibiotic effectiveness, reducing the length of stay and saving total direct medical costs by IDR 87,172.*

Keywords: *ceftriaxone, community-acquired pneumonia, cost-consequence, levofloxacin*

INTRODUCTION

Health problems are still a concern of the world, especially in developing countries such as ASEAN countries, including Indonesia. One of the diseases that is still a concern for the World Health Agency is pneumonia. Pneumonia is a major cause of death and hospitalization worldwide, as well as being a large user of healthcare resources and costs. The burden of health costs due to community-acquired pneumonia worldwide is enormous, and most of it is contributed by patient hospitalization costs (Peyrani *et al*., 2019). Pneumonia is still one of the most significant health problems for children under five years of age (toddlers) (Oktaria & Mahendradhata, 2022). Pneumonia, as an infectious disease in humans, also contributes to relatively high morbidity and mortality rates (Farida *et al*., 2020).

It is possible that pneumonia will still overshadow Indonesia's health year after year in view of the bacterial resistance and mutation of viruses nowadays, which are still a problem. The problem of bacterial resistance is also an essential issue in the field of public health in Indonesia. These health problems are a burden for countries, including Indonesia, which is currently still developing. In general, bacterial pathogens that cause Community-Acquired Pneumonia (CAP) include *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Staphylococcus aureus, Legionella species, Chlamydia pneumoniae, Moraxella catarrhalis* (Metlay *et al*., 2019). The emergence of *Methicillin-Resistant Staphylococcus Aureus* (MRSA) as a superbug (Nandhini *et al*., 2022) has drawn world attention to its handling and treatment costs, especially in pneumonia. The cost of treating antibiotic-resistant bacteria is undoubtedly increasing and becoming more expensive. Bacterial sensitivity test data at a Teaching Hospital in Surakarta City shows that the microorganisms that cause pneumonia in the hospital are *Streptococcus pneumoniae* (28%) followed by *Candida sp*. (21%), *Pseudomonas aeruginosa* (8.8%), *Klebsiella pneumoniae* (8.8%), and *Streptococcus viridans* (8.8%) where *Streptococcus pneumoniae* is sensitive to levofloxacin antibiotics (81.25%), ceftriaxone (62.5%), and ampicillin (75%) (Farida *et al*., 2019).

The cost of health care is the main concern of the Indonesian government through Badan Penyelenggara Jaminan Sosial (BPJS). The analysis of health costs has been paid attention to amidst the increasing cost of health in Indonesia. Pharmacoeconomics through cost-consequence analysis (CCA) can be a method for comparing the costs and consequences of applying a comparative drug to alternative drugs. Pharmacoeconomics can be a solution for health policymakers to determine the most rational drug therapy choice.

Pneumonia can attack anyone from young age to old age. WHO data from 2019 states that pneumonia was the cause of death in 14% of children under five. RISKESDAS 2018 data states that the prevalence of pneumonia in those aged 55 - 64 years is 2.5%, aged 65 - 74 years is 3.0%, and aged 75 years and over is 2.9% (Hatim, 2022). Data from the Central Statistics Agency of Surakarta (BPS) states that the number of pneumonia cases in Surakarta City in 2019 was 164 cases, in 2020 it was 178 cases, and in 2021 it was 262 cases (Dinas Kesehatan Kota Surakarta, 2022). The number of pneumonia cases has increased every year from 2019 to 2021. This is a concern on how to control the number of pneumonia cases so that they do not grow in number.

Pneumonia is a disease with a high burden in adults and is characterized by high morbidity (McLaughlin *et al*., 2020). The high cost of treatment and loss of productivity due to pneumonia is a significant economic burden for the government and the general public (Ekirapa-Kiracho *et al*., 2021). This makes it essential to do pharmacoeconomic evaluations for pneumonia to get the best therapy at an efficient cost.

Several recent economic evaluation studies regarding the use of antibiotics for pneumonia in hospitalized adult inpatients have been conducted by several researchers. Research at the Ajibarang Regional Hospital for the 2021 period concluded that giving ceftazidime antibiotic therapy was more cost-effective than ceftriaxone by comparing ACER values (Susanto *et al*., 2022). Research at RSU Karsa Husada, Batu City, from 2017 to 2018 found that the antibiotic levofloxacin was more cost-effective compared to ceftriaxone, cefotaxime and ciprofloxacin injections (Kolbiyah, 2019). Research at RST DD Hospital with adult inpatients found that the antibiotic ceftriaxone was more cost-effective than ceftizoxime for treating community-acquired pneumonia with indicators of the number of recovered patients and length of stay (Susanti *et al*., 2022). A Cost-Effectiveness Analysis study at the West Nusa Tenggara Provincial Hospital found that the antibiotic levofloxacin was more cost-effective than ceftriaxone for treating community-acquired pneumonia (CAP) (Rahmawati *et al*., 2023). The results of the study by Farida, Khoiry and Hanafi (2022) stated that the use of antibiotics for the treatment of pneumonia was ceftriaxone, levofloxacin, and the combination of ceftriaxone + azithromycin with the ACER value of the antibiotic levofloxacin was the most cost-effective

compared to ceftriaxone and the combination of ceftriaxone + azithromycin.

Pharmacoeconomic studies using the cost-consequence analysis method for community-acquired pneumonia (CAP) have not been widely done. The study by Torres *et al*. (2020) has done an economic analysis of ceftaroline fosamil compared to other antibiotics for community-acquired pneumonia therapy in hospitalized adult patients with moderate/severe CAP using the cost-consequence analysis method. It is known that ceftaroline fosamil can be an alternative therapy compared to ceftriaxone, levofloxacin and the combination moxifloxacin – co-amoxiclav because the total cost of treatment is lower and clinical outcomes are relatively better than comparators (Torres *et al*., 2020).

Levofloxacin and ceftriaxone are broad-spectrum antibiotics widely used as first-line empiric antibiotics for community-acquired pneumonia (Farida *et al*., 2020; Kresnawati *et al*., 2021; Rahmawati *et al*., 2023; Sukriya *et al*., 2022). The big difference in drug unit prices between levofloxacin and ceftriaxone for antibiotic therapy causes the total cost of hospitalization with levofloxacin to be more expensive than ceftriaxone (Aoralia, 2022). Pharmacoeconomic evaluation through cost-consequence analysis for using the alternative drug (ceftriaxone) with its comparator (levofloxacin) for community-acquired pneumonia therapy has yet to be done nowadays. This study aimed to describe the clinical and economic impact of administering ceftriaxone as a first-line empirical antibiotic compared to its comparator levofloxacin for community-acquired pneumonia therapy in hospitalized adult inpatients from the perspective of healthcare facilities.

MATERIALS AND METHODS
Method
Study design

This research is a retrospective observational study with a cohort method that collects data retrospectively. The sampling technique is total sampling, where all data that meets inclusion during the period of January to December 2022 is taken. This research was carried out from June until July 2023 at a secondary-care hospital in Surakarta. This research received ethical clearance from the Health Research Ethics Committee of Kusuma Husada Surakarta University with the number 119/UKH.L.02/EC/IX/2022.

The inclusion criteria of this study were hospitalized adult inpatients in third-class rooms$\geq$ 18 years old who were diagnosed with pneumonia with the ICD-10 code of J.12 - J.18 in the medical record (CAP

cases confirmation in this study was that patients with a discharge date $\leqslant$ 14 days before the index date were excluded from the study) (Konomura *et al*., 2017), patient was given levofloxacin or ceftriaxone injection as first-line empiric antibiotic therapy by the doctor at the time of initial hospitalization, self-paid and insurance (BPJS) category patients are all included because both of the direct medical costs are the same. The exclusion criteria for this study were patients with infections other than pneumonia (including COVID-19 positive), patients with severe comorbidities (cancer, immunocompromised, hematemesis melena), incomplete or missing medical record or patient billing, and patients who were forced to go home, died or referred to another hospital.

The data taken in this study were patient profiles, length of stay (LOS), antibiotic effectiveness and direct medical cost data. The patient profile includes age, gender and comorbidities. Length Of Stay (LOS) per antibiotic was determined by the patient being admitted to be hospitalized until they were allowed to go home by the doctor in charge. Antibiotic effectiveness was the antibiotic success rate of levofloxacin and ceftriaxone, which was defined as the ratio of the percentage of patients treated successfully (improved or cured) by levofloxacin or ceftriaxone antibiotic divided by the total number of patients given those antibiotics. The patient's treatment is stated to be successful (improved or cured) if the administration of levofloxacin or ceftriaxone as a first-line empiric antibiotic could improve the patient's clinical stability, marked by temperature $\leqslant$ 37.8C, pulse rate $\leqslant$ 100x/minute, respiratory rate $\leqslant$ 24x/minute, systolic blood pressure $\geqslant$ 90 mmHg, no requires oxygen supplements and can take oral medication and switching antibiotics from intravenous to oral. Besides, there is clinical improvement in one of four symptoms from baseline (cough, dyspnea, pleuritic chest pain, sputum production) with none worsening. The patient's treatment was stated to have failed if the patient did not achieve clinical stability and improvement and/or the antibiotic regimen was changed.

Direct costs were service costs, medication costs, and laboratory/diagnostic test costs. Service costs included room costs, medical procedures and doctor visits. Medication costs included costs of antibiotics, supporting drugs, pharmacy costs and consumables material. Laboratory/diagnostic test costs included costs for clinical laboratory tests (cost of electrolytes, blood counts, and blood chemistry test), diagnostic tests (chest

x-ray) and microbiological sensitivity tests if needed. All fees were calculated in Indonesian Rupiahs (IDR) and based on the hospital's perspective.

Research data will be analyzed using the cost-consequence analysis (CCA) method by comparing the effectiveness of antibiotics, length of stay and direct medical costs. The comparison of costs and their consequences will be displayed in tabular form and analyzed descriptively.

Study population

The population of this study were adult inpatients with community-acquired pneumonia (CAP) that are given levofloxacin or ceftriaxone antibiotics and were hospitalized at X Hospital Surakarta in third-class room at least one night in the period of January to December 2022. The sampling method was total sampling, which took all samples from January to December 2022 as long as they met the inclusion criteria.

Materials

This research requires two groups of data: patient medical records (MR) and direct medical cost data, which met the inclusion criteria from January to December 2022 at X Hospital Surakarta. The patient's medical record was used to get patient profiles and clinical data. Patient direct medical cost data was taken from the billing print-out of patient care costs at the hospital cashier. Patient cost data was the direct medical costs of patient care during hospitalization.

Tools

This research requires a data collection form that was made as a tool to help in collecting patient data. This research also used Microsoft Office Excel 2019 and SPSS version 20 software to analyse the data.

Data analysis

The data obtained was analyzed descriptively and presented in tables. Patient profile data (gender, age, comorbidities) were analyzed using the Chi-Square test if it met the requirements and the Fisher' 's Exact or Kolmogorov Smirnov test if it did not meet the Chi-Square test requirements. Outcome data, which were length of stay (LOS) and antibiotic effectiveness, were analyzed using the Chi-Square test if it met the requirements and Fisher' 's Exact test if it did not meet the Chi-Square test requirements. Cost data was presented by the unit value of the Indonesian Rupiahs (IDR), and the significance value was analysed using a student-t-test if the data were normal and a Mann-Whitney test if they were not. Data analysis was continued with sensitivity analysis by calculating the base-case value at its lowest and highest cost value for each direct medical cost (service cost, medication cost, and laboratory/diagnostic test cost) of levofloxacin and ceftriaxone antibiotics.

RESULTS AND DISCUSSION
Subject selection

There were 146 data of adult inpatients diagnosed with pneumonia who were hospitalized from January to December 2022 at X Hospital Surakarta. Exclusions included missing medical records (n = 4), patient died (n = 21), missing patient print-out billings (n = 7), infections other than pneumonia (n = 12), patient's age was less than 18 years old (n = 1), there were severe comorbidities (n = 20), the patient was hospitalized other than third-class room (n = 11), and the patient who were given other empiric antibiotics for first-line empiric treatment besides levofloxacin and ceftriaxone (n = 33). The sample screening flow is shown in Figure 1.

The samples that met the inclusion criteria and were taken as subjects in this study were 37 patients divided into two groups (levofloxacin and ceftriaxone groups). The levofloxacin group consisted of 23 samples, and the ceftriaxone group consisted of 14 samples. Levofloxacin and ceftriaxone are the antibiotics most commonly prescribed in cases of pneumonia or lower respiratory tract infections (Farida *et al*., 2022; Rahmawati *et al*., 2023).

Samples were selected based on predetermined exclusion criteria. A total of 4 patients had missing medical records. Twenty-one patients were deceased and had their medical records recorded. Seven patients' billing data had not been found. Twenty-two patients had infections other than pneumonia, including patients who tested positive for COVID-19. There was one patient aged less than 18 years. Ten patients had comorbidities that met the exclusion criteria. There were 11 patients hospitalized in rooms other than the third-class room. Thirty-three patients were given other empiric antibiotics as first-line antibiotic therapy besides levofloxacin and ceftriaxone.
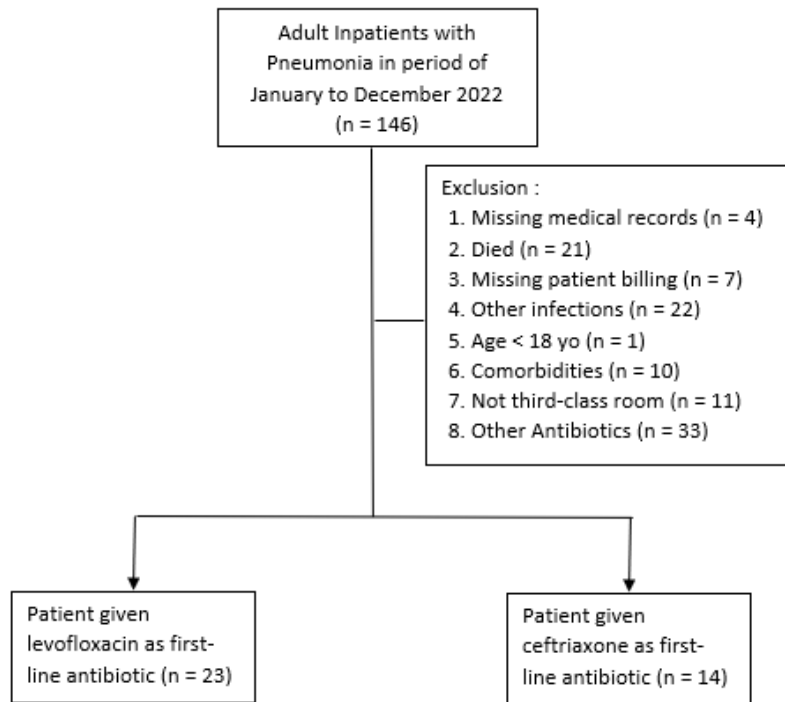
Figure 1. Sample screening flow

Patients with COVID-19 infections were not included in the study because COVID-19 is an infection by the SARS-CoV-2 virus that is different in general management from pneumonia (Bhimraj *et al*., 2022; COVID-19 Treatment Guidelines Panel, 2023; World Health Organization, 2021) and has an ICD-10 diagnosis code that is different from pneumonia, namely U07.1 (World Health Organization, 2019). COVID-19 disease has specific antiviral therapy treatment for the SARS-CoV-2 virus, including remdesivir, favipiravir or other antivirals with additional symptomatic therapy and administration of antibiotics if there are indications of bacterial infection (World Health Organization, 2021). Patients with comorbidities who were not included in this study were patients with comorbidity of cancer or tumours, liver disease and hematemesis melena. Cancer is a disease with high costs, many cases occurring, and high risk (Aisyah *et al*., 2018), so it was not included in this study. Meanwhile, liver diseases such as fatty liver, cirrhosis, which leads to variceal bleeding and hematemesis melena require expensive endoscopy procedures (Bakar, 2016) and, in some instances, require prophylactic antibiotics if the infection is indicated (Yoshiji *et al*., 2021). This study was limited to third-class room inpatients to limit variations in costs between inpatient room classes. The initial empirical antibiotic treatment included ampicillin-sulbactam, cefotaxime, ceftazidime, a combination of azithromycin and ceftriaxone, meropenem, a combination of cefuroxime and metronidazole, and a combination of azithromycin and levofloxacin. Cefuroxime was administered less frequently than levofloxacin and ceftriaxone.

Patient profiles

The descriptive data consisted of patient profiles that met the inclusion criteria in two groups, namely the levofloxacin group (23 patients) and the ceftriaxone group (14 patients), with a total of 37 patients. The patient profile was analyzed based on gender, patient age and comorbidities. Patient profiles can be seen in Table 1.

Patient gender profile data showed that there were 23 female patients more compared to 14 male patients. These results were in accordance with several previous studies where there were more women patients than men (Sukriya *et al*., 2022; Susanto *et al*., 2022). This result was different from other studies, which stated that the number of male patients dominated female patients (Farida *et al*., 2022; Susanti *et al*., 2022). The significance value (p-value) of gender data between the levofloxacin group and the ceftriaxone group was 0.365 (more than 0.05), so there was no significant difference between the two groups. The results of the gender data found that gender did not affect the prevalence of pneumonia because each region or hospital could have different results.

The result of age data showed that the total data for patients aged 51 - 60 years and 61 - 70 years were the

most significant number of adult patients hospitalized during the study period, with 11 patients each. These results show that patients aged 51 to 70 years were vulnerable to pneumonia. This data was similar to the results of research by Susanto *et al*. (2022), in which the most significant number of adult inpatients were aged 56 - 65 years. In another study, it was found that patients aged more than 56 years were susceptible to pneumonia in, more significant numbers than young adults (less than 56 years) (Farida *et al*., 2020). The significance value of patient age data showed that there were no significant differences between the two groups, with a p-value of 0.625 (more than 0.05). The results of patient age data found that patients aged over 50 years were more susceptible to pneumonia than younger people.

The most common comorbidities are cardiovascular disorders, respiratory disorders, and diabetes mellitus, with the number of cases being 18 patients, 16 patients, and 13 patients, respectively. Comorbidities of cardiovascular disorders and diabetes mellitus were suffered mainly through the ceftriaxone group sample. Meanwhile, comorbidities of respiratory disorders were primarily suffered mainly by the levofloxacin group sample. This was in accordance with research at an academic hospital in Sukoharjo that found that cardiovascular disorders, respiratory disorders, and diabetes mellitus occupied the most cases in pneumonia patients (Farida *et al*., 2020). In another study, it was found that the most common comorbidities in hospitalized adult pneumonia cases were cardiovascular disorders and respiratory disorders (Susanti *et al*., 2022).

Table 1. Pneumonia patient profiles of adult inpatients at X Hospital Surakarta period of January – December 2022

No	Patient Profiles	Levofloxacin (n = 23, %)	Ceftriaxone (n = 14) (%)	Total (n = 37) (%)	p-value*
1	**Gender**				
	Male	10 (43)	4 (29)	14 (38)	0.365[A]
	Female	13 (57)	10 (71)	23 (62)	
2	**Age (years old)**				
	18-20	0 (0)	0 (0)	0 (0)	
	21-30	0 (0)	0 (0)	0 (0)	
	31-40	0 (0)	1 (7.1)	1 (2)	
	41-50	1 (4)	3 (21.4)	4 (11)	
	51-60	9 (39)	2 (14.3)	11 (30)	0.625[C]
	61-70	9 (39)	2 (14.3)	11 (30)	
	71-80	2 (9)	2 (14.3)	4 (11)	
	81-90	2 (9)	2 (14.3)	4 (11)	
	91-100	0 (0)	2 (14.3)	2 (5)	
3	**Comorbidities**				
	Other respiratory disorders	14 (32)	2 (6)	16 (21)	0.006[A]
	Diabetes mellitus	5 (12)	8 (23)	13 (17)	0.039[B]
	Hypoglicemia	0 (0)	1 (3)	1 (1)	0.378[B]
	Cardiovascular disorders	6 (14)	12 (34)	18 (24)	0.000[A]
	Stroke	0 (0)	1 (3)	1 (1)	0.378[B]
	Hypokalemia	5 (12)	3 (8)	8 (11)	1.000[B]
	Hyponatremia	2 (5)	2 (6)	4 (5)	0.625[B]
	Increased transaminase	1 (2)	0 (0)	1 (1)	1.000[B]
	Urology disorders	4 (9)	4 (11)	7 (9)	0.445[B]
	Dyslipidemia	0 (0)	1 (3)	1 (1)	0.378[B]
	Hematology disorders	2 (5)	0 (0)	2 (3)	0.517[B]
	Gastrointestinal disorders	2 (5)	0 (0)	2 (3)	0.517[B]
	Thyroid disorders	1 (2)	0 (0)	1 (1)	1.000[B]
	Skin disorders	1 (2)	0 (0)	1 (1)	1.000[B]
	Hypoalbuminemia	0 (0)	1 (3)	1 (1)	0.378[B]

* Data from 37 patients who were hospitalized with a significance value (p-value) > 0,05 means there is no significant difference between the groups. A (Chi-Square Test), B (Fisher`s Exact Test), C (Kolmogorov-Smirnov Test)

Table 2. Length of stay patients

Length of Stay (LOS)	Levofloxacin (n = 23) (%)	Ceftriaxone (n = 14) (%)	Total (n = 37) (%)	p-value*
	average = 3.39 days	average = 3.00 days	average = 3.24 days	
1 - 4 days	20 (87)	14 (100)	34 (92)	0.275
5 - 8 days	3 (13)	0 (0)	3 (8)	

***Data from 37 patients who were hospitalized with a significance value (p-value) > 0,05 means there is no significant difference between the groups. P-value was determined using Fisher's Exact Test

Table 3. Antibiotic effectiveness of levofloxacin and ceftriaxone for the treatment of pneumonia

Antibiotic effectiveness	Failure (n = 7)	Success (n = 30)	Success percentage (%)	p-value*
Levofloxacin (n = 23)	6	17	75 %	0.217
Ceftriaxone (n = 14)	1	13	93.33 %	

*The significance value (p-value) was analyzed using Fisher's Exact test

The significance value of comorbidities was less than 0.05 for cardiovascular disorders, respiratory disorders, and diabetes mellitus, with p-values of 0.000, 0.006, and 0.039, respectively. This means that there was a significant difference (p-value less than 0.05) between the levofloxacin and ceftriaxone groups in terms of comorbid data on cardiovascular disorders, respiratory disorders and diabetes mellitus. Comorbid cardiovascular disorders and diabetes mellitus were most commonly suffered by patients in the ceftriaxone group. In another study, it was found that the highest usage of the ceftriaxone antibiotic (the highest DDD) was given to patients with cardiovascular disease along with diabetes mellitus and hypokalemia (Sukriya *et al*., 2022). Other research also states that ceftriaxone was often given to respiratory infection cases in South India (Sriram *et al*., 2013). Doctors' preferences in giving antibiotics to their patients influence the antibiotics used. Comorbid respiratory disorders occurred more frequently in patients in the levofloxacin group. This might be because levofloxacin is the fluoroquinolone antibiotic of choice for respiratory disorders *(Metlay et al*., 2019; Perhimpunan Dokter Paru Indonesia, 2014). Other research also found that the antibiotic levofloxacin was often given to adult pneumonia inpatients with comorbid respiratory disorders (Farida *et al*., 2020). It was found that there were no significant differences between other comorbidities between the two drug groups, with a significance value of more than 0.05.

The patient's length of stay (Table 2) was calculated using the length of stay (LOS) parameter obtained from medical record data with a length of stay of 1 to 4 days, totalling 34 patients and 5 to 8 days, totalling three patients. This data was similar to other similar studies in that the length of stay for most patients was five days or less in the levofloxacin and ceftriaxone groups (Farida *et al*., 2020; Putri; *et al*., 2018). The significance value (p-value) for the two antibiotic groups was 0.275, which means that there was no significant difference in the length of stay data for the levofloxacin group and the ceftriaxone group. However, if the average length of stay was calculated, it was found that the ceftriaxone group had the shortest average length of stay at 3.00 days compared to the levofloxacin group with 3.39 days. This means that patients in the ceftriaxone group went home sooner than those in the levofloxacin group.

Antibiotic effectiveness for pneumonia

Antibiotic effectiveness was determined using the antibiotic success rate parameters presented in Table 3. The success rate for antibiotics in the levofloxacin group with successful therapy was 17 patients, while failed therapy was six patients with a success rate percentage of 75%. The antibiotic success rate for the ceftriaxone group was 13 patients with successful therapy and one patient with failed therapy, with a success rate percentage of 93.33%. The significance value (p-value) was 0.217, which means that there was no significant difference between the two antibiotic groups. This followed the results of previous research that the effectiveness of levofloxacin and ceftriaxone as first-line empirical antibiotics was statistically the same (Rahmawati *et al*., 2023). The antibiotic success rate was different from the results obtained in other studies where the success rate of levofloxacin was higher than ceftriaxone (Farida *et al*., 2022; Sukriya *et al*., 2022). This might be caused by different comorbidities in each other group, which can affect the outcome of the success rate of both antibiotics (Sukriya *et al*., 2022). This difference also might be due to different germ resistance patterns in the hospitals where the research was carried out.

Table 4. Direct medical costs of pneumonia of adults inpatients in X Hospital Surakarta

	Levofloxacin (n = 23)		Ceftriaxone (n = 14)		p-value*
	Cost	Percentage (%)	Cost	Percentage (%)	
Average service cost	IDR485,609	23.6	IDR602,857	30.6	0.481
Average medication cost	IDR1,267,799	61.6	IDR945,199	48.0	0.008
Average laboratory/diagnostic test cost	IDR303,391	14.8	IDR421,571	21.4	0.012
Average total cost	IDR2,056,799	100	IDR1,969,627	100	0.079

* Significance value (p-value) was analyzed using the Mann-Whitney test

Table 5. Cost-consequence analysis (CCA) of levofloxacin and ceftriaxone group for pneumonia therapy

Antibiotic Groups	Therapeutic effectiveness	Effectiveness Difference	Length of stay (LOS)	LOS difference	Total direct medical cost	Cost difference
Levofloxacin (reference)	75.00%		3.39 days		IDR 2,056,799	
Ceftriaxone (alternative)	93.33%	-18,33%	3.00 days	0.39 days	IDR 1,969,627	IDR 87,172

Cost of pneumonia therapy

Direct medical costs (Table 4) are divided into three cost groups, which are service costs, medication costs, and laboratory/diagnostic test costs. Service cost data showed that the average cost for the levofloxacin group was IDR 485,609 with a percentage of 23.6% of the average total cost, and the ceftriaxone group was IDR 602,857 with a percentage of 30.6% of the average total cost. The significance value for the service cost group showed a p-value of 0.481, so there was no significant difference between the two groups. Service costs were the costs of services provided by the hospital while the patient is hospitalized.

Medication cost data showed that the average cost for the levofloxacin group is IDR 1,267,799 with a percentage of 61.6% of the total cost, and the ceftriaxone group is IDR 945,199 with a rate of 48.0% of the total cost. The significance value for the medication cost group showed a p-value of 0.008, which means there was a significant difference in medication costs between the two groups. Medication costs were all costs for administering medication to patients along with disposable materials during hospitalization, including the medications the patient takes home.

Laboratory/diagnostic test cost data showed that the average cost in the levofloxacin group was IDR 303,391 with a percentage of 14.8% of the total costs, and in the ceftriaxone group, was IDR 421,571 with a percentage of 21.4% of the total costs. The significance value in the medical cost group showed a p-value of 0.012, which means there was a significant difference in laboratory/diagnostic test costs between the two groups. Laboratory/diagnostic test costs were all laboratory/diagnostic test costs related to pneumonia for patients, such as chest x-ray costs, blood cell counts and electrolytes.

The average total cost was the summation of the average service costs, medication costs and laboratory/diagnostic test costs per antibiotic group. In the levofloxacin group, it was found that the average total cost was IDR 2,056,799. In the ceftriaxone group, it was found that the average total cost was IDR 1,969,627. The significance value was obtained with a p-value of 0.079, which means there was no significant difference in the average total cost between the two antibiotic groups.

The medication costs for the levofloxacin group were more expensive than those for the ceftriaxone group and were significantly different between both groups based on the p-value. The high cost of medication in the levofloxacin group was caused by the cost of levofloxacin antibiotics, which were much more expensive than the cost of ceftriaxone antibiotics. In addition, the high cost of medication in the levofloxacin group was supported by the cost of corticosteroid infusion drugs such as hydrocortisone infusion. In the ceftriaxone group, the high cost of medication was caused by the cost of other drugs than ceftriaxone itself, such as albumin infusion, insulin and complementary drugs cost. This was in accordance with other studies that found that the average total direct cost of levofloxacin is higher than ceftriaxone (Sriram *et al*., 2013).

Laboratory/diagnostic test costs in the ceftriaxone group were higher than those of the levofloxacin group and were significantly different between both groups based on the p-value. The higher laboratory/diagnostic test costs in the ceftriaxone group were due to the cost of blood chemistry tests being more frequent in the

ceftriaxone group compared to levofloxacin. Blood chemistry tests carried out on pneumonia patients include inflammatory biomarker tests and blood gas analysis (Julianti *et al*., 2023). Apart from that, blood chemistry tests also included checking blood glucose and lipids. The number of patients with cardiovascular comorbidities in the ceftriaxone group might have influenced the cost of blood chemistry tests.

It showed that laboratory/diagnostic test costs were more expensive in the ceftriaxone group than in the levofloxacin group (p-value 0.012). Meanwhile, medication costs were more expensive in the levofloxacin group compared to the ceftriaxone group (p-value 0.008).

Cost consequence analysis (CCA)

The cost-consequence analysis (CCA) of the levofloxacin and ceftriaxone groups for community-acquired pneumonia therapy can be seen in Table 5.

The therapeutic effectiveness of the ceftriaxone group was higher than that of the levofloxacin group, with a difference of 18.33%. This means that using levofloxacin as a first-line empirical antibiotic caused a reduction in the therapeutic effectiveness of community-acquired pneumonia therapy by 18.33% compared to ceftriaxone, but this was not statistically significantly different (p-value = 0.271).

Length of stay can be a consequence of administering antibiotics in an infection therapy. In the levofloxacin group, the average length of stay for inpatients in the hospital was 3.39 days. In the ceftriaxone group, the average length of stay for inpatients in the hospital was 3.39 days. In the levofloxacin group, it was shown that administration of levofloxacin had the consequence of increasing the length of stay for community-acquired pneumonia patients who were hospitalized by 0.39 days longer than

the ceftriaxone group. However, this is not statistically significantly different (p-value 0.275).

The difference in total direct medical costs in the levofloxacin group and the ceftriaxone group was IDR 87,172. This shows that administering levofloxacin to adult community-acquired pneumonia patients hospitalized in hospitals had the consequence of increasing costs by IDR 87,172. Hospitals could save IDR 87,172 if they use ceftriaxone as the first-line empirical antibiotic for community-acquired pneumonia therapy in hospitalized adult patients instead of levofloxacin. This was different from the results of other studies that stated that levofloxacin is more cost-effective than ceftriaxone (Farida *et al*., 2022; Kolbiyah, 2019; Rahmawati *et al*., 2023). Differences in results occurred because, in those studies, the effectiveness of levofloxacin was higher than that of ceftriaxone, resulting in more cost-effectiveness.

Sensitivity analysis

Sensitivity analysis was done to determine the sensitivity of the direct medical costs to the cost difference between both groups so that the influence of uncertainty and robustness can be estimated. Sensitivity analysis is presented in Table 6. Sensitivity analysis was conducted by determining the lowest and highest costs for each service cost, medication cost, and laboratory/diagnostic test cost in the levofloxacin and ceftriaxone groups.

In the sensitivity analysis, it was found that changes in service costs, medication costs, and laboratory/diagnostic test costs in the levofloxacin and ceftriaxone groups could change the cost difference value. These results suggested that changes in the direct costs of either the levofloxacin or ceftriaxone groups can change the cost difference value. Changes in each direct medical cost of both antibiotics were sensitive to changes in the cost difference value.

Table 6. Sensitivity analysis

	Sensitivity Analysis		Levofloxacin cost	Ceftriaxone cost	Cost difference
			IDR 2,056,799	IDR 1,969,627	IDR 87,172
Ceftriaxone	Service costs	lowest IDR 263.000	IDR 2,056,799	IDR 1,187,425	IDR 869,374
		highest IDR 1,501,000	IDR 2,056,799	IDR 3,844,974	IDR -1,788,175
	Medication costs	lowest IDR 442,461	IDR 2,056,799	IDR 1,076,461	IDR 980,338
		highest IDR 2,330,342	IDR 2,056,799	IDR 4,177,342	IDR -2,120,543
	Laboratory/Diagnostic test costs	lowest IDR 166,000	IDR 2,056,799	IDR 1,076,461	IDR 980,338
		highest IDR 814,000	IDR 2,056,799	IDR 4,177,342	IDR -2,120,543
Levofloxacin	Service costs	lowest IDR 308,000	IDR 1,470,335	IDR 1,969,627	IDR -499,292
		highest IDR 1,318,000	IDR 4,593,087	IDR 1,969,627	IDR 2,623,460
	Medication costs	lowest IDR 778,466	IDR 1,693,466	IDR 1,969,627	IDR -276,161
		highest IDR 2,708,087	IDR 4,593,087	IDR 1,969,627	IDR 2,623,460
	Laboratory/Diagnostic test costs	lowest IDR 65,000	IDR 1,366,155	IDR 1,969,627	IDR -603,472
		highest IDR 671,000	IDR 2,560,207	IDR 1,969,627	IDR 590,580

This study has several limitations. This study is a retrospective study with a small sample size and was conducted in one hospital. Therefore, there are limitations in measuring effectiveness and may not represent a representative sample. This study also only estimates direct medical costs. Indirect costs like loss of productivity and absence of family or caregivers are not analysed.

CONCLUSION

In conclusion, there were different consequences in community-acquired pneumonia therapy for adult inpatients who used levofloxacin and ceftriaxone as first-line empirical antibiotics. We found that administering ceftriaxone than levofloxacin as a first-line empirical antibiotic therapy for community-acquired pneumonia in hospitalized adult patients had the consequences of increasing the therapeutic effectiveness by 18.33%, reducing the length of stay in the hospital by 0.39 days and saving total direct medical costs by IDR 87,172 per community-acquired pneumonia case in hospital. Although the results of several previous studies have differences, the use of first-line empirical antibiotics for community-acquired pneumonia in adult inpatients requires further pharmacoeconomic evaluations.

ACKNOWLEDGMENT

AUTHOR CONTRIBUTIONS

Conceptualization, R.R., M.S.I., H.A.C.S.; Methodology, R.R., H.P.A., M.S.I., R.N.F., E.; Software, R.R., A.W.A., J.S.; Validation, H.P.A., M.S.I.; Formal Analysis, R.R., H.A.C.S.; Investigation, R.R., A.W.A., J.S., H.A.C.S.; Resources, R.R., J.S.; Data Curation, R.R., H.A.C.S.; Writing - Original Draft, R.R., A.W.A., H.A.C.S.; Writing - Review & Editing, J.S., E., R.N.F.; Visualization, R.R., J.S.; Supervision, H.P.A., M.S.I., R.N.F.; Project Administration, R.R., H.P.A., M.S.I., R.N.F.; Funding Acquisition, R.R., H.P.A., M.S.I., R.N.F.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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