# Analysis of Cost Effectiveness of Beta–Lactam Antibiotics in Child Pneumonia Patients

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**Abstract.** Pneumonia has a high rate of morbidity and mortality. The costs associated with treating pneumonia are high, ranging from 254 to 1,208 USD in Indonesia. The adequate use of antibiotics can help reduce high costs. Pharmacoeconomic studies were conducted to determine the effectiveness of the patients' treatment costs, one of which was Cost Effectiveness Analysis (CEA), which was used in making decisions on the selection of the best alternative in the selection of treatment costs. This study aims to analyze the most cost-effective antibiotics in pneumonia patients at the Bekasi City General Hospital. This study is descriptive research that uses observation with retrospective data collection and uses the CEA method. Data taken in the form of medical records of pneumonia patients aged 0 months to 5 years. Samples were taken of as many as 100 patients who met the inclusion and exclusion criteria. Based on the results of the ACER value, the effectiveness of the ceftriaxone is higher with a lower cost, compared to cefotaxime with the results of lower effectiveness and higher costs. The ACER results for ceftriaxone cost IDR 39,706/day and cefotaxime IDR 122,571/day. Therefore, it can be concluded that the use of ceftriaxone in pediatric pneumonia was the most cost-effective at Bekasi City General Hospital in 2019-2020.

**Keywords:** Pneumonia; Children; Antibiotics; CEA

## 1 Introduction

Pneumonia is a common disease and one of the highest causes of death in the world. Pneumonia attacks infants and children as the body's defense system in infants and children is not yet perfect which makes it easily defeated by infecting microorganisms (Juwita, 2017). In 2017, the mortality rate of children under 5 years was 808,694 people (WHO, 2019). Based on the results of basic health research in 2018, the death rate caused by pneumonia was 1,017,290 people (Ministry of Health Indonesia, 2019). Pneumonia in infants and children is quite high where the mortality of children under-five ranks number 2 in Indonesia (Baharirama Virgo, 2017).

Pneumonia has a high level of morbidity and mortality (Prina E., 2015) The costs associated with treating pneumonia are high (Welte T., 2012), which ranges from 254 to 1,208 USD in Indonesia (Azni S., 2016). The adequate use of antibiotics can help prevent pneumonia and reduce the high costs. (Carratala J., 2012).

Treatment of pneumonia patients is generally carried out with empirical antibiotic therapy, namely the beta-lactam group (Postma D.F., 2015). Different types of beta-lactam antibiotics result in different effectiveness and costs. It thus needs an analysis from the side of pharmaconomy that involves cost and effectiveness reviews. The pharmacoeconomic concept conducted in this study was a cost-effectiveness analysis with the aim of determining the most cost-effective option between ceftriaxone and cefotaxime. The parameter measured was a decrease in body temperature (36.5 °C - 37 °C).

An increase in temperature can exacerbate and heighten the risk of death in pneumonia patients, whereby a decrease in body temperature can be a clinical outcome in pneumonia patients. (Blot M., 2014) The perspectives used in this study were payer perspective (BPJS, Social Health Insurance Administration Body) and healthcare perspective (hospital). Afterwards, an analysis of the most influential factors on the value of cost-effectiveness was carried out. The purpose of this study was to analyze the most cost-effective antibiotics in pneumonia patients at the Bekasi City General Hospital.

## 2 Methodology

This research is a descriptive study that uses observation with retrospective data collection and uses the CEA (Cost Effectiveness Analysis) method. Sampling was conducted with total sampling. The data were taken from the patients' medical and financial records at the Bekasi City General Hospital, including patients' characteristics data (medical record number, patient's initials, age, and gender), patients' clinical data (diagnosis and body temperature check), drug use data (dose, instructions for use, and the duration of drug administration), and data on total treatment costs (healthcare perspective: treatment costs, examination fees, drug costs, medical device costs, hospitalization costs, and doctor service fees; payer perspective: Indonesian-Case Based Groups/INA-CBG rates).

*Sample and sample criteria*
The samples were non-ICU inpatients who were also children under five with a diagnosis of pneumonia at the Bekasi City General Hospital. The inclusion criteria were patients who completed data records, used BPJS, had a main diagnosis of pneumonia (children who are 0 months to 5 years old), and have been hospitalized for at least 2 days. The exclusion criteria were pneumonia patients under five years old that have ended the treatment period on their own request or were forced to go home with uncontrolled conditions, patients who were allergic to penicillin antibiotics, patients who died during treatment, patients with complications of other diseases, and patients with other infectious diseases.

*Data Analysis*
In this study, the total direct medical costs were used, namely all costs incurred by patients to receive treatment while being hospitalized at the Bekasi City General Hospital. The total direct medical costs and drug effectiveness were then analyzed by the CEA method using ACER and ICER calculations (Setiawan, 2017). ACER is the average of the direct treatment costs of each treatment divided by the percentage of therapeutic effectiveness. Meanwhile, ICER is defined as the ratio of the difference between the costs of the two alternatives in terms of its effectiveness and is calculated based on the equation (Andayani, 2013).

# 3   Results and Discussion

The results obtained as many as 100 samples and were classified based on the type of antibiotic therapy for pneumonia patients at the Bekasi City General Hospital, namely ceftriaxone and cefotaxime using the Intravenous Pathway.

*Characteristics Data of Pneumonia Patients*

**Table 1.** Based on the Characteristics of Respondents

| Characteristics of Respondents | Number of Patients | Percentage (%) |
|---|---|---|
| Gender | | |
| Female | 39 | 39 |
| Male | 61 | 61 |
| Age | | |
| 0-1   Years | 51 | 51 |
| 2-5   Years | 49 | 49 |
| Treatment Time | | |
| 2 - 4 Days | 85 | 85 |
| 5 - 7 Days | 13 | 13 |
| 8 - 10 Days | 1 | 1 |
| 11 - 13 Days | 1 | 1 |

The results of this study are in accordance with research conducted by Amalia, which obtained 60% male and 40% female (Lanang Amelia, 2018). Factors affecting pneumonia that occur in male inpatients include the diameter of their respiratory tract that are smaller than that of women which is indicated by chest pain and affects the endurance or immunity of the individuals (Hartati, et al., 2012). The female lungs have good and higher airflow resistance so as to allow air circulation to run smoothly in the respiratory cavity, thereby protecting the lung organs from pathogenic infections (Lanang Amelia, 2018).

The results of this study were in accordance with the results of Yelfi Anwar's research where pneumonia patients aged 0-1 years is 63.4%, compared to 30.46% of patients aged 2-5 years (Anwar Yelfi, 2016). The age of 0-1 year is an age that is susceptible to infectious diseases, especially pneumonia compared to the age of 2–5 years. This is due to an immature immune system which causes the body's resistance to infectious diseases to become more vulnerable, such as pneumonia infection. Toddlers who are born prematurely have a high risk of diseases related to immunity, the central nervous system, and lungs because the reflux of sucking, swallowing, and coughing is not perfect yet (Hartati et al., 2012). Pneumonia can be infected through polluted air, a dirty environment, as well as cigarettes which can be inhaled by children directly and cause breathing problems.

In addition, inadequate breastfeeding and nutritions at the age of under 5 years can affect the immune system of toddlers and children. For toddlers, in the condition that the immunization is not complete, they will be more prone to get attacked by infected diseases through breathing infected air that will enter the respiratory tract and cause pneumonia. Giving immunization can prevent viruses, bacteria, and foreign objects that can potentially contribute to being infected with infectious diseases, including pneumonia (Hasnawati, 2018).

The length of treatment is one of the factors that can be used to measure the effectiveness of drug use and to describe the average treatment time for pneumonia patients. In general, the average pneumonia hospitalization at the Bekasi City General Hospital is 4 days. This study is

in accordance with Nita Tanti's research, which demonstrates that the length of treatment is 76.66%. The length of stay of the patient can be seen in the length of the patients' treatment in the hospital, whereby the faster the treatment in the hospital is, the faster the recovery would be. Antibiotics and supporting drugs can help treat patients during hospitalization. Effective antibiotic therapy is used for a maximum of less than 10 days, so most patients have been allowed to go home after receiving hospital treatment for 10 days and their clinical signs improved (Farida Yeni et al., 2017).

*Antibiotics and Health Service Security*

**Table 2.** Antibiotics and Social Security Status

| Room | | Antibiotics Used in Pneumonia Patients | | | Percentage |
|---|---|---|---|---|---|
| | Inpatient | Ceftriaxone | Cefotaxime | Total | (%) |
| BPJS | Class I | 24 | 10 | 34 | 34% |
| | Class II | 15 | 9 | 24 | 24% |
| | Class III | 27 | 15 | 42 | 42% |
| | Total | 66 | 34 | 100 | 100 |

Pneumonia therapy is carried out by giving antibiotics which aims to eradicate the microorganisms that cause pneumonia. Based on Table 3, the antibiotics use at the Bekasi City General Hospital for the period 2019 to September 2020 was dominated by the ceftriaxone drug with a total of 66 patients and by cefotaxime drug as many as 34 patients. The use of antibiotics in children at the Bekasi City General Hospital is dominated by the use of single antibiotics. The results of this study are in accordance with Silvia Monica's study, where the use of antibiotics in pediatric hospitalized patients is dominated by single antibiotic treatment, namely ceftriaxone as many as 63 patients and cefotaxime as many as 50 patients (Monica Silvia et al., 2018).

Ceftriaxone and cefotaxime are types of third-generation cephalosporin antibiotics that have characteristics to be broad spectrum, have gram-negative activity, and are actively attacking S. Pneumoniae. Cephalosporins penetrate body fluids and tissues effectively, which can be used to treat a wide variety of severe infections caused by organisms that are resistant to almost all other antibiotics. The third-generation cephalosporin antibiotic is widely used in patients with pneumonia whose cause is unknown (Musdalipah, 2018). The research conducted by Made Virgo is mostly pathogenic for Community Acquired Pneumonia, especially S. Pneumonia which is the bacteria that causes it to be found in children and toddlers (Baharirama virgo Made, 2017).

The Bekasi City General Hospital chose the antibiotic ceftriaxone for the first treatment of pneumonia in toddlers and children, which is not in accordance with WHO that explains the treatment of pediatric patients with severe pneumonia should be given Ampicillin 20-25 mg/kg intravenously or intramuscularly every 6 hours which will be observed during the first 72 hours. For severe pneumonia patients who cannot receive oral medication, the Indonesian Pediatric Association (IDAI) recommends that the use of antibiotics is done through the intravenous route, namely ampicillin and chloramphenicol, co-amoxiclav, ceftriaxone, cefotaxime, and cefuroxime (Pudjiadi A et al., 2009). This is not in accordance with what is used by the Bekasi City General Hospital. The choice of antibiotics at the Bekasi City General Hospital is the same as that described by Eka Kartika's research where for children under 1 year of age the use of ceftriaxone via the intravenous route has the advantage of a long elimination half-life compared

to cefotaxime. Therefore, it is sufficient to give it once a day. Ceftriaxone works by inhibiting the synthesis of microbial cell walls and transpeptidase enzymes, which are inhibited at the time of cell wall formation (Eka Kartika Untari et al., 2014).

Based on Table 2, the use of cefotaxime and ceftriaxone in Class I treatment rooms are given to 34 patients, then to 24 patients in Class 2, and to 42 patients in Class 3. In general, it is a fact that patients with BPJS who are classified into Class 3 are higher in number, compared to Class 1 and 2. The class depends on the family's ability to pay health insurance. Nevertheless, patients can still have the right to get proper treatment and facilities from the hospital.

*The Use of Non-Antibiotic Drugs*

In the treatment of pediatric pneumonia patients, besides being given antibiotics which are the main therapy, supporting drugs are also given which is expected to help improve the patients' quality of life and speed up the healing process

**Table 3.** Characteristics of Non-Antibiotic Drug Use

| Therapy Class | Medicine Name | Amount | Percentage |
|---|---|---|---|
| Nebulizer | Ventolin + Nacl | 39 | 39% |
| | Ventolin | 21 | 21% |
| Analgesic And Antipyretic | Paracetamol | 87 | 87% |
| Ca iran Electrolytes | KAEN 3A | 68 | 68% |
| | Ring Lactate | 32 | 32% |
| Anti Inflammation | Dexamethasone | 26 | 26% |
| Adrenergic Bronchodilators | Salbutamol | 71 | 71% |
| Anti Diarrhea | Lacto –B | 10 | 10% |
| Mucolytic | Ambroxol | 39 | 39% |
| | Vestein | 12 | 12% |
| Antiemetic | Ondansentron | 10 | 10% |
| Stomach Ulcer | Ranitidine | 9 | 9% |
| Antihistamines | Cetirizine | 17 | 17% |

Based on Table 3, it can be seen that the most widely used non-antibiotic drugs at the Bekasi City General Hospital among toddlers and children are analgesics and antipyretics that are amounted as much as 86%, adrenergic bronchodilators (71%), and IV fluids or electrolyte fluids KAEN 3A (68%). These treatments help the healing process and relieve symptoms in pneumonia patients. Analgesics and antipyretics are given to the inpatients who have fever. Meanwhile, adrenergic bronchodilators are used in patients who suffer from coughs that interfere with the respiratory system. Therefore, adrenergic bronchodilator drug therapy is given to help the healing process. The inpatients are also assisted with an infusion device containing electrolyte fluid whose functions are to restore tissue perfusion and hydration.

*Cost Effectiveness Analysis*
1)  Antibiotic Unit Price Profile

**Table 4.** Antibiotic Unit Price

| Antibiotic Name | Administration Route | Price Per Unit (IDR) |
|---|---|---|
| Ceftriaxone | Intravenous | 5,885/Vial |
| Cefotaxime | Intravenous | 5,603/ Vial |

Based on Table 4, each type of antibiotic has a different price per vial. The administration of antibiotics is used in hospitalized patients who are members of National Health Insurance (BPJS). This health service ensures that patients who are sick will get the services they need without considering their economic situation. This study also analyzes the patients who possess BPJS or other health insurances.

Based on the analyzed data, there were more patients with BPJS than independent or general patients. Treatment of patients at the Bekasi City General Hospital with BPJS uses generic antibiotics. The selling price of branded generic drugs is usually more expensive than the selling price of generic drugs because they are packaged more adequately and promotions are carried out intensively (Sugiarto, 2014). The administration of antibiotics in hospitals through the parenteral route would help drug destruction or inactivation in the gastrointestinal tract, making the drug effect to be felt in a quick manner (in an emergency). However, parenteral preparations also have disadvantages, one of which is the high price due to the complex manufacturing process (Syamsuni, 2006).

2)  Direct Medical Expenses

Direct medical costs for pediatric pneumonia patients hospitalized at the Bekasi City General Hospital in the period 2019 to September 2020 consisted of eleven types of financing, namely the cost of antibiotic and non-antibiotic drugs, laboratory fees, inpatient costs, doctor services fees, emergency room costs, BMHP fees, room costs, nursing services, radiology costs, and treatment costs.

**Table 5.** Data on Direct Medical Costs by Type of Antibiotic Therapy

| TYPE COSTS | CEFTRIAXONE (in IDR) | | | CEFOTAXIME (in IDR) | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| Maintenance | 80,651,820 | 46,024,915 | 63,426,700 | 31,135,890 | 25,185,200 | 34,437,981 |
| Inpatient | 17,550,000 | 7,230,000 | 8,970,000 | 5,850,000 | 5,865,000 | 5,557,000 |
| Non-antibiotic | 8,790,629 | 3,800,795 | 7,543,905 | 2,821,925 | 2,328,734 | 3,896,880 |
| Antibiotics | 447,260 | 1,794,205 | 488,095 | 140,075 | 123,266 | 207,371 |
| Doctor's visit | 5,557,500 | 2,835,000 | 4,642,500 | 2,066,250 | 1,717,500 | 2,782,500 |
| Treatment | 8,925,750 | 6,528,500 | 6,805,500 | 3,576,750 | 3,888,750 | 4,249,000 |
| Nursing services | 3,312,000 | 1,707,750 | 2,732,000 | 1,333,000 | 931,500 | 1,527,500 |
| Radiology | 2,340,000 | 1,462,500 | 2,632,500 | 950,000 | 877,500 | 1,462,500 |
| Laboratory | 3,163,000 | 2,028,000 | 4,374,000 | 1,107,000 | 1,255,000 | 1,511,001 |
| BMHP | 1,678,590 | 1,062,290 | 2,019,520 | 692,640 | 610,750 | 1,318,980 |
| Emergency Room | 12,573,200 | 9,023,750 | 14,803,650 | 5,711,250 | 4,643,950 | 7,628,500 |
| Total direct medical costs | 144,989,749 | 83,497,705 | 118,438,370 | 55,384,780 | 47,427,150 | 60,330,213 |
| Total average | 31,447,802 | | | 14,831,103 | | |

Based on Table 5, direct medical costs for hospitalized pneumonia patients at the Bekasi City General Hospital were classified by drug class and BPJS class level. There are differences in direct costs for each patient group due to direct medical costs consisting of laboratory costs, pharmaceutical costs, medical personnel costs, and other costs (room costs, treatment costs, etc.). The only difference is the class and condition of the patients during hospitalization. The

results of the total direct medical costs for treatment while at the hospital with the antibiotic ceftriaxone were dominated in Class 1 with a total direct medical cost amounted to IDR 144,989,749. It was followed by Class 3 patients with the same drugs, namely ceftriaxone, with a total direct medical cost of IDR 118,438,370, and the last one is patients in Class 2 using ceftriaxone with a total direct medical cost of IDR 83,497,705.

The total number has been added up from all direct medical costs while the patients were being treated at the Bekasi City General Hospital. Meanwhile, the use of cefotaxime dominated in Class 3 with a total direct medical cost of IDR 60.330.213. This is because inpatients at the Bekasi City General Hospital who are BPJS Class 3 patients are being administered with cefotaxime. The cost was then followed by patients in Class 1 with a total direct medical cost of IDR 55,384,780, while Class 2 patients with cefotaxime treatments cost IDR 47,427,150.

Based on the results of the average total direct medical costs taken from eleven direct medical data or the cost of treating patients while being hospitalized at the Bekasi City General Hospital, when viewed from the type of drug class, the usage of ceftriaxone and cefotaxime sequentially dominates. Meanwhile, when viewed based on the BPJS class level, Class 1 patients with the ceftriaxone drug group dominate. This is due to differences in the number of patients, the cost of hospitalization of patients in hospitals, as well as room facilities, care, and length of stay of patients while in hospital.

3) Antibiotic effectiveness

Effectiveness is the achievement of therapeutic targets or changes in the patients' health condition with health interventions from a clinical practice. It will be said to be effective if the results of the intervention are in accordance with the expected results. In this study, the target achieved was measured by the body temperature of the Bekasi City General Hospital. According to the Indonesian Pediatrician Association (IDAI), the body temperature of a child is normally in the range of 36.5 – 37°C (A Pudjiadi et al., 2009).

**Table 6.** Effectiveness of Antibiotics in Pneumonia Patients

| Antibiotic | Number of Patients | Number of Patients Reaching Target Body Temperature | Therapy Effectiveness (%) |
|---|---|---|---|
| Ceftriaxone | 66 | 47 | 72% |
| Cefotaxime | 34 | 22 | 64% |

Based on Table 6, the effectiveness of antibiotics used by Bekasi City General Hospital for children with ceftriaxone was 72% with a normal body temperature target of 47 patients and cefotaxime was 64% with a normal body temperature of 22 patients.

4) Cost Effectiveness Analysis

Cost effectiveness analysis is an analysis in Pharmacoeconomics that can be used to determine which intervention is the most efficient in treatment with the minimum cost to achieve the desired expenditure by comparing two or more interventions (Wulandari, 2019). In the research, the effectiveness analysis uses the ACER and ICER methods. ACER is the cost needed to increase the effectiveness of each treatment, while ICER is the cost of treatment that must be incurred to increase effectiveness by switching from one treatment to another (Andayani, 2013).

**Table 7.** ACER Calculation Results

| Antibiotic | Average total cost Effectiveness (IDR) (C ) | Therapy Effectiveness (%) ( E ) | Acer (IDR) ( C/ E) |
|---|---|---|---|
| Ceftriaxone | 2,858,891 | 72% | 39,706 |
| Cefotaxime | 1,348,282 | 64% | 122,571 |

Based on Table 7, the ACER results describe the total cost of a program or alternative divided by clinical outcomes, where costs are divided by therapeutic effects. In this study, the ACER formula is a direct medical total which is differentiated based on the type of antibiotic therapy given to pneumonia patients. Meanwhile, the effectiveness is taken from the number of patients who have normal body temperature outcomes in infants and children or in other words, when the patients' body temperature has been determined safe to go home.

ACER results are defined as average cost per unit of effectiveness. The smaller the ACER value, the more cost-effective the drug will be. It is known that the antibiotic therapy with the highest to the lowest ACER value was cefotaxime with IDR 122,571, and with ceftriaxone value of IDR 39,706. Based on the calculation results, the ACER is known to be a single antibiotic therapy, namely ceftriaxone antibiotic from cefotaxime antibiotic therapy. Ceftriaxone which is more cost effective than cefotaxime antibiotic therapy was given to inpatient pneumonia patients under five and children at the Bekasi City General Hospital in 2019 to 2020.

**Table 8.** Comparison of Therapeutic Effectiveness – Cost of Antibiotic Therapy

| Cost Effectiveness | Lower Cost | Same Cost | Higher Cost |
|---|---|---|---|
| Lower effectiveness | A (Need ICER calculation) | BB | C (Dominated) CEFOTAXIME |
| Same effectiveness | D | E | F |
| Higher effectiveness | G (Dominant) CEFTRIAXONE | H | I (Need ICER calculation)) |

Based on Table 8, there is a relationship between the effectiveness of antibiotic therapy and the cost of antibiotic therapy in pneumonia patients at the Bekasi City General Hospital for the period of 2019 to 2020, where there are two types of single antibiotics which are divided into 2 groups, namely position G which is the antibiotic ceftriaxone located in the dominant column and position H which is the antibiotic cefotaxime in the dominant column. The G position is ceftriaxone which has lower cost with higher effectiveness. Meanwhile, cefotaxime at H has

lower effectiveness with higher costs. It can be concluded that the beta lactam class of antibiotics has different activities.

The results of these two antibiotic therapies are in different positions and therefore does not require CEA (Cost Effectiveness Analysis) calculation. Ceftriaxone in position G has higher health interventions with lower costs. This intervention is included in the dominant quadrant and can be the main choice, while cefotaxime, which has higher costs and low health interventions, is not eligible to be the main choice (Didik, 2017). Ceftriaxone is the drugs that are cost effective with a price of IDR 39,706/day compared to cefotaxime which is priced at IDR 122,571/day.

## 4    Conclusion

The most effective use of antibiotics at the Bekasi City General Hospital for pneumonia was ceftriaxone and the total average direct medical cost with ceftriaxone was at IDR 31,447,802, while cefotaxime was at IDR 14,831,103. The average results of the use of antibiotics with ACER, namely ceftriaxone, can be considered cost effective at the Bekasi City General Hospital with an average cost of IDR 39,706/day while cefotaxime stood at IDR 122,571/day.

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