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The most cost-economist used of antibiotics in COVID-19 patients: cost-minimization analysis study in hospital

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Abstract

Background: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is the cause of COVID-19, a respiratory disease. One of the treatments administered to COVID-19 patients is antibiotics to prevent the occurrence of secondary infections. However, the budget allocation for antibiotic use issued by health facilities constitutes a considerable amount due to the significantly high demand, particularly among COVID-19 patients. This situation calls for pharmacoeconomic studies, such as cost-minimization analysis, for a better understanding and management of the financial implications.

Objective: This study aimed to assess the economic value of antibiotics in a hospital within Tangerang District in 2021.

Method: The method used in this study was non-experimental observation through the retrospective analysis of secondary data, consisting of patient costs and demographic information. The sample was selected based on inclusion and exclusion criteria. Furthermore, the collected data were analyzed using the Kruskal-Wallis test to determine a significant difference between the total cost in each therapy group.

Results: In this study, 30 patients' data met the inclusion and exclusion criteria consisting of 4 groups: ceftriaxone (n=10), cefixime (n=10), ceftazidime (n=7), and cefadroxil (n=3). Based on the calculation of cost-minimization analysis, the total average cost per patient for the ceftriaxone, cefixime, ceftazidime, and cefadroxil groups was 19,853,503 IDR, 13,330,545 IDR, 38,666,056 IDR, and 21,333,330 IDR, respectively.

Conclusion: The results showed that the cefixime group has the most economical value.

Keywords: Antibiotics, cost-minimization analysis, COVID-19, hospital

1. Introduction

The health sector is increasingly becoming a major focus globally due to the first outbreak of COVID-19 (Corona Virus Disease 2019) in Wuhan, China. This disease is caused by the severe acute respiratory syndrome virus, CoronaVirus-2 (SARS-CoV-2), which is part of the coronavirus type. According to the World Health Organization (WHO), COVID-19 is classified as a Public Health Emergency of International Concern (PHEIC) (Julaiha, *et al.* 2023).

COVID-19 has experienced a rapid spread across various countries around the world. As of December 3, 2021, a total of 263,563,622 COVID-19-positive cases and 5,232,562 deaths were recorded. During this period, Indonesia reported 4,257,243 cases. and 143,858 deaths (WHO, 2021). According to a multicentre cross-sectional study conducted in China, 80% of SARS-CoV-2 patients had mild to moderate symptoms similar to those of other viral respiratory infections (Wu *et al*., 2020).

In the early stages of COVID-19, patients presented with bacterial pneumonia, accompanied by common symptoms such as coughing, fever, and choking sensations (Huang *et al*., 2020; Zhao *et al.,* 2020). Additionally, the patients are at risk of developing bacterial co-infection, which often leads to death. Previous studies have shown that viral and bacterial infections cause an increase in the mortality rate (Guo *et al.,* 2019; Wang *et al.*, 2020). According to COVID-19 patient management guidelines, antibiotics play a crucial role in preventing and managing secondary infections (Burhan *et al*., 2020).

The administration of antibiotics for bacterial infection treatment requires precision, emphasizing the need for accuracy. To ensure effective antibiotic use, several considerations are needed, including cost-effectiveness, efficiency, toxicity, and theability to minimize resistance (Amin, 2014). A multicentre study conducted in China showed that 58% of COVID-19 patients received antibiotics intravenously (Chen *et al.,* 2020). Similarly, another report found that more than 70% of patients received antibiotics, with 25% receiving single antibiotics and 45% being administered combinations (Chen *et al.*, 2020). The process of administering antibiotics depends on several factors, including early manifestations of COVID-19 similar to community-acquired pneumonia (CAP), secondary bacterial infection, absence of specific antivirals, and high mortality rates (Huttner *et al.*, 2020).

The selection of drug alternatives is significantly diverse, requiring pharmacological knowledge and economic aspects to opt for affordable options with optimal therapeutic outcomes. Cost-minimization analysis (CMA) is an analytical tool for comparing the cost of different health interventions to identify the most cost-effective alternative with similar outcomes. When two or more therapies (type, brand) are equivalent in clinical outcomes, the comparison is only made on intervention cost. According to the principle of economic efficiency, the type or brand of medicine offering the best value by incurring the least cost is considered the preferred option. Pharmacoeconomic studies, particularly cost-minimization analysis on COVID-19 patients, are still limited in referral hospitals for COVID-19 patients in the Tangerang district. Consequently, this study aimed to analyze and minimize the cost associated with antibiotic use in COVID-19 patients in hospital located in the Tangerang district.

2. Method

2.1 Research design, perspective, and sample target

This study used a non-experimental observational method with a cross-sectional design. A pharmacoeconomic analysis was carried out using the cost-minimization analysis method, which focused on comparing two or more groups of interventions to identify the least or most economical group (Arnold, 2021). From a patient perspective, this study considered the cost of the party responsible for the treatment (Kemenkes RI, 2017). Consequently, the direct medical cost covering various aspects was used for analysis, including consultation, visits, laboratory, radiology, operation, therapy, medication, single-use pharmaceutical supplies, equipment rental, room rental, and service.

The target population in this study included COVID-19 patients hospitalized in one hospital in the district of Tangerang. The data used was obtained from those who met the inclusion and exclusion criteria. The inclusion criteria were the characteristics of the subject in the target population and the accessible population (Sastroasmoro, 2018). These included COVID-19 patients receiving single antibiotic therapy, having complete cost data, aged 15-64, and patients declared recovered and allowed to return by a doctor. Meanwhile, the exclusion criteria were characteristics present in subjects who met the inclusion criteria but possessed attributes that could be intrusive or interfering (Patino & Ferreira, 2018). The exclusion criteria were COVID-19 patients receiving combination antibiotic therapy or an overhaul of the type, having incomplete cost data, patients sent home, and those who died. The data used were obtained from inpatients exposed to COVID-19 for the period January-December 2021, consisting of both patients and cost data.

2.2 Data collection

Secondary and retrospective data were collected using a purposive, non-probability sampling method based on pre-determined criteria (Isaac, 2023). Moreover, secondary data are information available before the start of a study and can be analyzed (Unachukwu *et al.*, 2018). Retrospective data were obtained from past times (Talari & Goyal, 2020) and grouped according to antibiotic therapy group, consisting of patient characteristics (gender and age) and cost details.

2.3 Data analysis

2.3.1 Cost Minimization Analysis (CMA)

This study aimed to determine which antibiotic therapy had the lowest cost compared to others using a cost-minimization analysis formula.

Total cost = fixed cost + variable cost

Fixed cost : hospitals and administrative costs

Variable cost : COVID-19 treatment costs, supportive treatment costs, and medical costs

2.3.2 Data statistics analysis

The collected data were analyzed statistically using SPSS Version 27 to determine significant differences between the two variables. Subsequently, the normality test assesses whether the distribution of the residual value is normal. For parametric methods, it is essential that the data be distributed normally. However, when the data is not normally distributed, nominal, or ordinal, the method used is non-parametric statistics. In this study, the Kolmogrov-Smirnov test was used to determine normal data distribution ($p < 0.05$). When the normality test results show a normal data distribution, the next test uses a parametric one-way ANOVA test. For nominally distributed data, a non-parametric test is carried out Kruskal-Wallis.

3. Result and discussion

3.1 Sociodemographic of COVID-19 patients

After data collection, 30 samples that met the inclusion and exclusion criteria were obtained. The collected and proposed samples were presented based on characteristics and cost-minimization analysis. The characteristics that were considered included age, gender, and therapeutic groups, as shown in Table 1.

Table 1. Sociodemographic frequency distribution of COVID-19 patients

Characteristics	Frequency	Percentage (%)
Sex		
Male	16	53.3
Female	14	46.7
Total	30	100
Age		
15-24 years	3	10
25-34 years	3	10
35-44 years	5	16.7
45-54 years	11	36.7
55-64 years	8	26.7
Total	30	100
Therapy groups		
Cefadroxil	3	10
Cefixime	10	33.3
Ceftazidime	7	23.3
Ceftriaxone	10	33.3
Total	30	100

Age and gender are the risk factors for COVID-19 and death. In this study, the majority of samples were male, as presented in Table 1, which was consistent with Yusransyah *et al.* (2022), who identified 53% male and 47% female. In some countries, such as Pakistan, the majority of cases of COVID-19 patients consisted of 72% males (Adams, 2020), which was similar to a case report in Canada (Lochlainn *et al.*, 2020; Stall *et al.*, 2020). This showed the potential increase in COVID-19 cases and deaths among male patients in different countries (Villa *et al.*, 2020; Wenham *et al.*, 2020). The male gender is considered a risk factor for COVID-19 due to differences in sexual behavior, ACE2 (Angiotensin-Converting Enzyme 2) differential expression, and sex hormones between males and females (Kelada *et al.*, 2020).

The process of viral infection is significantly influenced by receptor expression and distribution (Zhao *et al.*, 2020). The SARS-CoV-2 virus can be delivered by the ACE-2 receptor (Cao *et al.*, 2020). Therefore, increasing the number of ACE-2 receptor expressions can increase the chances of SARS-CoV-2 virus pathogenesis. Among male patients, the number of ACE-2 gene expressions is higher compared to females, thereby increasing the infection risk (Zhao *et al.*, 2020).

Age is also a risk factor for COVID-19, with the majority of samples in this study being 45-64 years old. According to Yusransyah *et al.* (2022), the majority of samples were 51-64 years old, followed by 40-50 years old. According to Meister *et al.* (2022) analysis of Estonia, the majority of the samples were between the ages of 30-39 and 40-49. This showed that the incidence of COVID-19 is prevalent in the age range of 30-64 years.

The National Vital Statistics System (NVSS) stated that when compared to the ages of 18-29 years old, the risk of death in the 50-64 year age group is 25 times higher, 140 times higher than 65-74 years, and 340 times greater than those above 85 years (CDC, 2023). The risk of increased severity in COVID-19 patients can occur at all ages based on primary health conditions and patients over 50 (Ahmad *et al.*, 2023).

3.2 Cost

The samples in this study were patients hospitalized in inpatient 4-bedded and 6-bedded rooms. The pharmacoeconomic perspective used was the patient, and the cost data for purchase was the direct medical cost. The entire cost of all samples was covered by the Indonesian government through the Health Insurance Organizing Agency program (BPJS Kesehatan).

The normality test results for cost data referred to a p-value of 0.004, showing that the data were not distributed normally. Therefore, the next statistical test used a non-parametric test, the Kruskal-Wallis test, to identify significant or non-average differences in total direct medical cost per patient between antibiotic therapy groups. Table 2 shows details of the direct medical cost of each therapeutic group in this study.

Table 2. Average direct medical cost data

Cost type	Cefadroxil (IDR)	Cefixime (IDR)	Ceftazidime (IDR)	Ceftriaxone (IDR)
Consultations and visits cost	1,198,333	1,874,500	3,277,857	1,792,500
Laboratory	420,397	1,770,801	3,044,359	1,863,026
Radiology cost	108,000	138,600	120,857	467,000
Treatment and therapy cost	966,678	1,623,698	4,291,465	2,202,064
Medicine cost	492,061	2,422,740	8,860,457	3,831,159
Single use pharmaceutical cost	7,744,860	3,539,206	12,603,918	6,641,793
Rent tools cost	21,333	185,500	1,544,167	974,466
Service and other cost	165,000	351,000	855,000	504,350

Cost type	Cefadroxil (IDR)	Cefixime (IDR)	Ceftazidime (IDR)	Ceftriaxone (IDR)
Rent room cost	1,216,667	1,424,500	4,288,571	1,913,500
Cost-minimization analysis	**21,333,330**	**13,330,545**	**38,666,056**	**19,853,503**

Consultation costs and visits are high in the ceftazidime group and low in the cefadroxil group. The laboratory cost for the cefadroxil group was the lowest nominal cost, while ceftazidime had the highest. The nominal radiological cost was highest in the ceftriaxone group, and the lowest was found in the cefadroxil group. Operation and therapy costs in the cefadroxil group were the lowest nominal operation and treatment costs. Furthermore, operation and therapy costs in the ceftazidime group represent the highest nominal costs. The cost of medical expenditure was high in the ceftazidime group, and the lowest was found in the cefixime group. The nominal service and other costs were highest in the ceftazidime group, while they were lowest for the cefadroxil group. The highest cost of renting a large device was in the ceftazidime group, and the lowest cost was found in the cefadroxil. The nominal rental cost of the room was highest in the ceftazidime group, while the lowest was cefadroxil.

The cost of using the drug included antibiotics and other drugs. The ceftazidime group had the highest cost, while cefadroxil in the therapeutic group had the lowest cost of medication, as presented in Table 2. The cost of antibiotics in cefadroxil, cefixime, ceftazidime, and ceftriaxone is 679 IDR/tablet, 495 IDR/tablet, 13,632 IDR per ampoule, and 3,514 IDR/ampoule, respectively.

After performing calculations using the cost-minimization analysis formula, the average value of the total cost per patient in each group was obtained. The statistical results of the Kruskal-Wallis test showed a significance of 0.011, or less than 0.05, indicating a significant difference in the total average cost in each therapeutic group. However, the values obtained were influenced by differences in sample size, the patient's severity, and the length of stay.

This study used pharmacoeconomic methods, namely cost-minimization analysis, to compare two or more total costs of health interventions with the same outcomes. The four groups of antibiotic therapy are given to COVID-19 patients with similar health outcomes, namely preventing and/or curing secondary infections that may occur when hospitalized. Based on distribution, the cefixime and ceftriaxone groups had 10 samples, the ceftazidime group consisted of 7, and the cefadroxil group comprised 3.

In this study, the cost-minimization analysis formula summarizes total treatment, focusing on direct medical costs. Details of direct medical expenses consist of nine-unit costs, including consultation, visits, laboratory, radiology, operation, therapy, medication use, medical equipment usage, equipment rental, service, room rent, and other charges. Based on cost details of each group, the cost unit with the highest nominal value in all therapeutic groups was medical supplies. In terms of cost of drug use, the cefadroxil group had the lowest, while ceftazidime had the highest. According to the price of antibiotics in each group, ceftazidime had the highest, while cefixime had the lowest. Based on the concept of cost-minimization analysis, the therapeutic group was the most economical, with the lowest average total cost per patient. Therefore, cefixime was the most economical therapeutic group because it had the lowest nominal average patient total cost compared to other antibiotic therapies. The difference in the quantity of samples and locations had an impact on the results. The difference in the quantity of samples and locations had an impact on the results.

4. Conclusion

In conclusion, this study explored the use of four antibiotic therapies for treating COVID-19 patients in a hospital in the district of Tangerang, including cefixime, ceftazidime, ceftriaxone, and cefadroxil. Based on calculations using the cost-minimization analysis formula, the cefixime group was the most economical therapeutic group compared to others.

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