COST-EFFECTIVENESS ANALYSIS USE OF ANTIBIOTICS IN COVID-19 PATIENTS

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ABSTRAK

Corona Virus Disease 2019 (Covid-19) merupakan penyakit menular yang disebabkan oleh severe acute respiratory syndrome corona virus 2 (SAR-CoV-2) dan dapat menyebabkan infeksi saluran pernafasan. Penyakit ini membutuhkan biaya besar dalam proses penatalaksanaanya. Hal tersebut berdampak terhadap kondisi ekonomi pasien, sehingga diperlukan identifikasi studi farmakoekonomi. Salah satu metode farmakoekonomi yang dapat digunakan yaitu yaitu Cost Effectiveness Analysis, metode tersebut digunakan untuk memilih serta menghitung biaya terapi dan manfaat (outcome) yang paling baik pada beberapa pilihan terapi untuk tujuan yang sama. Penelitian ini bertujuan untuk menganalisis nilai cost-effectiveness penggunaan antibiotik azitromisin dan levofloksasin pada pengobatan Covid-19 di RSU Fastabiq Sehat PKU Muhammadiyah Pati. Pengambilan sampel dalam penelitian ini dilakukan secara purposive sampling. Sampel yang diperoleh sesuai kriteria inklusi sebanyak 57 pasien. Data diambil dari rekam medis pasien, instalasi farmasi dan keuangan meliputi data karakteristik, data, data penggunaan obat, data total biaya pengobatan. Biaya ditinjau dari biaya langsung medis (direct medical cost). Efektivitas terapi pasien COVID-19 di RSU Fastabiq Sehat PKU Muhammadiyah Pati yang mencapai target adalah kelompok antibiotik azitromisin dengan presentase (80,76%). Nilai ACER menunjukan antibiotik azitromisin sebesar Rp.97.809 dan levofloksasin sebesar Rp. 127.285. Model terapi yang dapat dijadikan standar pengobatan COVID-19 yaitu azitromisin di RSU Fastabiq Sehat PKU Muhammadiyah Pati.

Kata Kunci: Antibiotik, *Cost Effectiveness analysis*, Covid-19

ABSTRACT

Corona Virus Disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SAR-CoV-2) and can cause respiratory tract infections. This disease requires a large cost in the management process. This has an impact on the economic condition of the patient, so it is necessary to identify pharmacoeconomic studies. One of the pharmacoeconomic methods that can be used is Cost-Effectiveness Analysis, this method is used to select and calculate the best therapeutic costs and benefits (outcomes) for several therapeutic options for the same purpose. This study aims to analyze the cost-effectiveness of using the antibiotics azithromycin and levofloxacin in the treatment of COVID-19 at the Fastabiq Sehat General Hospital, PKU Muhammadiyah Pati. Sampling in this study was carried out by purposive sampling. Samples obtained according to the inclusion criteria were 57 patients. The data was taken from the patient's medical records, pharmaceutical installations, and finances including characteristics, drug use data, and data on total medical costs. Costs are reviewed from direct medical costs (direct medical costs). The effectiveness of therapy for COVID-19 patients at Fastabiq Sehat General Hospital PKU Muhammadiyah Pati reached the target in the antibiotic azithromycin group with a percentage (80.76%). The ACER value showed the antibiotic azithromycin was Rp.97,809 and levofloxacin was Rp. 127,285. The therapy model that can be used as

a standard treatment for COVID-19 is azithromycin at the RSU Fastabiq Sehat, PKU Muhammadiyah Pati.

INTRODUCTION

Coronavirus Disease 2019 (Covid-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a new type of coronavirus that has never been previously identified in humans (Burhan et al., 2020). Common symptoms that arise include symptoms of acute respiratory disorders such as fever, cough, and shortness of breath. The average incubation period is 5-6 days with the longest incubation period being 14 days. Cases of Covid-19 that are included in the severe category can cause pneumonia, acute respiratory syndrome, kidney failure, and death (RI Ministry of Health, 2020d). Specific therapy or treatment for Covid-19 cases has not been found (BPOM, 2020), however, the spread of the disease is very fast and causes the death rate to increase. Efforts are being made to provide therapy to Covid-19 patients using vitamins,

Antibiotics are drugs that are prescribed to almost all patients diagnosed with Covid-19 (Sinto, 2020). Antibiotics that are often used in Covid-19 patients include Azithromycin and Levofloxacin. Azithromycin is a macrolide antibiotic that can prevent severe respiratory infections in pneumonia patients (Bacharier & Leonard, 2015). Levofloxacin is a broad-spectrum fluoroquinolone antibiotic that fights several pathogenic bacteria that cause pneumonia (Raini, 2016). According to the Indonesian Ministry of Health (2023), antibiotics cannot be used as a means of prevention or treatment in Covid-19 patients, however, antibiotics are often given because of a secondary infection caused by bacteria. Therefore, the effectiveness of therapy and the amount of costs required for patient care are not known with certainty.

Economic evaluation is an analytical technique for comparing two or more techniques related to costs and outcomes. Economic evaluation can assist in making certain policy decisions (Andayani, 2013). Economic evaluation techniques with cost analysis are quite diverse, the appropriateness of the type of analysis depends on the purpose, availability of data, and other sources. The process of identifying and calculating all the costs and benefits of outcomes is very important to do (Paluseri et al., 2021). One of the economic evaluation techniques that can be done is Cost Effectiveness Analysis (CEA). CEA is a pharmacoeconomic method for selecting and assessing the best program or drug for several therapeutic options with the same goal. CEA is not only seen from the cheapest cost but also based on cost optimization (Rahayu et al., 2013). Based on the description above, it is necessary to conduct research on the Cost-Effectiveness Analysis of Antibiotic Use in Covid-19 Patients at the Fastabiq Sehat General Hospital, PKU Muhammadiyah.

METHOD
Research design

This research was carried out using a purposive sampling technique. Purposive sampling is a sampling technique based on predetermined inclusion criteria. The data used in this research is secondary data. The data was obtained from the patient's medical records and financial information at the Fastabiq Sehat General Hospital, PKU Muhammadiyah Pati, where the data to be used includes patient characteristic data (medical record number, patient initials, age, gender, length of stay, and co-morbidities), patient clinical (diagnosis and swab-test results), drug use data (azithromycin and levofloxacin), data on total medical costs in terms of direct medical costs incurred while in the care of Covid-19 patients (laboratory costs, radiology, drugs, inpatient installation).

Population and Sample

The population in this study were patients diagnosed with Covid-19 at the Fastabiq Sehat Hospital, PKU Muhammadiyah Pati, where it was known that the number of patients was 328 patients. Based on this population, the sample was determined using inclusion criteria. Samples taken must meet the criteria, which include: inpatients with a diagnosis of COVID-19 who either recovered or died in the period May-June 2021, received antibiotic treatment with azithromycin and levofloxacin, had complete information (age, co-morbidities, sex, date of in and out, drug therapy given). Patients who met these criteria were 57 patients.

Data analysis

The data in this study were grouped into 2 groups, namely the azithromycin and levofloxacin use groups. The data obtained were analyzed using Microsoft Excel to determine patient characteristics, cost-effectiveness of therapy, and total cost of therapy in terms of direct medical cost. The effectiveness and total cost of therapy can be determined by the following formula:

$$\text{Effectiveness of therapy} = \frac{\text{Patients Recovered}}{\text{Total Patients}} \times 100\%$$

$$\text{Total Cost} = \text{Drug cost} + \text{Radiology cost} + \text{Laboratory cost} + \text{Hospitalization cost}$$

Effectiveness data and the total cost of therapy that has been calculated are used to determine the value Average Cost Effectiveness Ratio (ACER). This value indicates the cost of the most effective therapy and is calculated using the following formula:

$$\text{ACER} = \frac{\text{Total Cost}}{\text{Effectiveness of therapy}}$$

RESULT AND DISCUSSION
Patient characteristics

COVID-19 is seen from gender, age, comorbidities, and length of stay. Based on the data obtained, it is known that the number of COVID-19 patients is the highest, namely men with 30 patients (52.63%) compared to women with 27 patients (47.37%) which can be seen in Table 1. This is because men ignore protocols more health, and have a smoking habit. In line with Agus' research (2020) which states that men in Indonesia are more susceptible to exposure to COVID-19 than women. Women tend to be more concerned about environmental conditions and their health. Other research states that women also have better knowledge about preventing COVID-19 compared to men. There is concern about being exposed to COVID-19 which is currently high, causing women to be more disciplined in maintaining cleanliness by implementing health protocols in the new normal period (Nawangsari, 2021).

Table 1. Gender

No	Gender	Frequency	Percentage (%)
1	Woman	27	47,37
2	Man	30	52,63
	Total	57	100.00

Based on the age category, the highest percentage of patients diagnosed with Covid-19 was aged 46-65 years (59.65%), while the lowest percentage was aged 17-25 years (7.02%).

The highest number of patients was in the age range of 46-65 years as many as 34 patients, where this age was included in the classification of middle age to elderly elderly (Dyussenbayev, 2017). This is because the elderly experience a decrease in body functions due to the aging process, in which almost all organ functions and movements decrease, followed by decreased immunity as body protectors, and accompanied by comorbidities.

One of the factors for this incident is possible because the elderly have a weaker immune system. As a result, the elderly are unable to fight infections that enter the body, including COVID-19. The elderly also tend to have many health problems that can increase the severity of their condition when exposed to Covid-19 (Elviani et al., 2021). This can be prevented by adopting good habits or living a healthy life. This habit has the most influence on preventing the behavior of exposure to Covid-19, where the better the habit, the easier it is for the elderly to avoid Covid-19 (Nurwanto, 2021).

Table 2. Patient Age

No	Age	Frequency	Percentage (%)
1	17-25	4	7.02
2	26-45	14	24.56
3	46-65	34	59.65
4	66-100	5	8.77
Total		57	100

Patient characteristics were also seen from the co-morbidities of patients with Covid-19, where based on the data obtained it showed that the highest percentage was in patients suffering from Diabetes Mellitus (33.33%). The problem faced by Diabetes Mellitus sufferers is complications that are worse when exposed to Covid-19 diabetes. This risk can be smaller for people with diabetes mellitus who can manage their condition properly (Hikmawati & Setiyabudi, 2020; Guo et al., 2020), while the lowest percentage is in Covid-19 patients with co-morbidities, namely Cutaneous Neurofibroma (7.01%). Neurofibroma is the most common neoplasm in the nervous system, tumor cells never experience malignant growth (Yulian et al., 2018). According to research by Ardizzone et al., (2022) Covid-19 patients accompanied by rare diseases, including neurofibromas, sufferers need good care so that they are not life-threatening.

Table 3. Concomitant Diseases

Code	Concomitant Diseases	Frequency	Percentage (%)
0	There isn't any	14	24.56
1	Asthma	10	17.54
2	DM (Diabetes Millitus)	19	33.33
3	IHD(ischemic heart disease)	5	8.77
4	CNF(Cutaneous Neurofibroma)	4	7.02
5	CHF(Congestive heart failure)	5	8.77
Total		57	100

Patients exposed to Covid-19 are known to have different lengths of treatment for each patient. Based on the data obtained, it shows that the length of stay for Covid-19 patients < 10 days has the highest percentage of 57.89%, compared to the length of stay > 10 days of 42.11%. The length of treatment for Covid-19 depends on the severity of the patient's condition while undergoing hospitalization. This is because the incubation period for Covid-19 is estimated to be between 1 and 14 days, and this estimate may change as cases develop. This is in line with research conducted in China which showed that the length of stay for Covid-19 patients ranged from 4 to 53 days, and that of ICU patients ranged from 6 to 12 days (Rees et al., 2020).

Table 4. Length of Treatment

Code	Length of Treatment	Azithromycin	Lefofloxacin	Total	Percentage (%)
1	4-10 days	14	19	33	57.89
2	>10 days	12	12	24	42.11
Total				57	100

Therapeutic Effectiveness Analysis

The cost of using antibiotics in Covid-19 patients is seen in direct medical costs, where the total costs can be seen in Table 5. Based on this table it shows that the costs of Covid-19 patients who are hospitalized receive antibiotic drug therapy azithromycin and levofloxacin. The total cost for patients receiving azithromycin antibiotic therapy was 205,376,287, while the total cost for levofloxacin antibiotics was 229,095,692. Covid-19 patients who received azithromycin antibiotic therapy were known to be 26 patients and levofloxacin in 31 patients. The results can be seen in Table 6. Based on these data, the average total cost of azithromycin therapy for each patient was 7,899,087 and levofloxacin was 7,390,183.

Table 5. Total Cost of Using Azithromycin and Levofloxacin

Parameter	Group Azithomycin(Rp)	Levofloxacin Group (Rp)
Drug Cost	1,663,223	4,011,183
Maintenance costs	170,870,714	186,740,759
Laboratory Fees	24,864,350	30,707,692
Radiology Fees	7,978,000	7,639,500
Total cost	205,376,287	229,095,692
Average	7,899,087	7,390,183

The effectiveness of antibiotic therapy can be seen in Table 6, where the percentage of azithromycin was 80.76% and levofloxacin was 58.06%. Based on these results it can be concluded that the use of the antibiotic azithromycin is more effective and has a lower death rate compared to levofloxacin. These results are consistent with research by Paluseri et al., (2021) which stated that the effectiveness of azithromycin was higher with a percentage of 96% compared to levofloxacin with a percentage of 93%.

Table 6. Therapeutic Effectiveness

No	Drug Class	Number of Patients	Number of Patients Died	Number of Patients Cured	Percentage (%)
1.	Azithromycin	26	5	21	80,76
2.	Levofloxacin	31	13	18	58.06

Cost Effectiveness Analysis of Therapy

Cost-effectiveness can be used to facilitate decision making which treatment has the best effectiveness in the cost-effectiveness analysis method (Andayani, 2013). Table 7 shows that the ACER (Average Cost Effectiveness) value in the azithromycin group is lower than that in the levofloxacin group in terms of the total medical cost of each patient (direct medical cost). The azithromycin therapy group had an ACER value of 97,809 which means that for every 1% increase in effectiveness, it costs 97,809. Azithromycin has a high total medical cost for each

patient compared to levofloxacin, but azithromycin has good effectiveness compared to levofloxacin. Therefore, it can be concluded that azithromycin is more effective in curing Covid-19 patients and minimizes lower mortality compared to levofloxacin. According to Paluseri et al., (2021), the azithromycin antibiotic therapy group is more cost-effective in the treatment of Covid-19 compared to the levofloxacin antibiotic therapy group.

Table 7. ACER values

No	Antibotic Group	ACER (C/E)
1.	Azithromycin	97,809
2.	Levofloxacin	127,285

Azithromycin is an antibiotic that is widely used for the treatment of Covid-19 patients (Lisni et al., 2021). The use of azithromycin can reduce viral load (estimated rate of viral replication in the body) in Covid-19 patients. The decision to use azithromycin must weigh the potential benefits and risks. The effectiveness of a drug seen from the benefits provided is greater than the risks that arise (Donsu & Hasmono, 2020). Azithromycin is known as an antibacterial drug, but it is also known to interfere with the entry of viruses into host cells and increase the immune response against viruses (Yanti, 2021). The antibiotic azithromycin is the main choice in the treatment of Covid-19 patients which is recommended for the management of Covid-19 patients (Lisni et al., 2021).

Therapy using the two antibiotics showed different results. Therapy using levofloxacin is known to have a low total medical cost for each patient with low effectiveness. The ACER value in the levofloxacin therapy group was 127,285, which means that every 1% increase in effectiveness requires a cost of 127,285. This is due to the low effectiveness of therapy which results in many patients dying, so the costs of intervention are getting higher (Paluseri et al., 2021). Patients on levofloxacin therapy due to the severity of Covid-19 and experiencing acute respiratory distress syndrome (ARDS), ARDS increases the risk of death in Covid-19 patients, and occurs at an advanced age (Kelana et al., 2021).

CONCLUSION

Patients diagnosed with COVID-19 at the Fastabiq Sehat Hospital, PKU Muhammadiyah Pati, based on gender, were mostly male (52.63%) and aged 46-65 years (31.58%). The most comorbid disease is DM (Diabetes Mellitus) as much as 33.33%. The effectiveness of therapy for COVID-19 patients at Fastabiq Sehat General Hospital PKU Muhammadiyah Pati reached the target in the azithromycin group with a percentage of 80.76%. This antibiotic is the most cost-effective antibiotic with an ACER value of 97,809, so this group can be used as a standard treatment for COVID-19 at the Fastabiq Sehat General Hospital, PKU Muhammadiyah Pati.

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