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Research Article

Cost-effectiveness analysis of cefazolin and clindamycin in postpartum patients at PKU Muhammadiyah Hospital Yogyakarta

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ABSTRACT

Postpartum infections can occur after normal or cesarean delivery. Proper administration of antibiotics can reduce the risk of postpartum infection The occurrence of postpartum infections can increase the cost of childbirth. The purpose of this study is to find out the cost-effectiveness of antibiotic therapy at PKU Muhammadiyah Hospital Yogyakarta. This study was retrospective observational and was conducted during October to December 2020. The inclusion criteria in this study were postpartum patients who received cefazolin and clindamycin therapy and were over 20 years old, while the exclusion criteria in this study were patients who died, had incomplete data, and had complications of the disease. The effectiveness of antibiotic therapy was measured from the clinical outside of body temperature and length of hospitalization. Cost-effectiveness were assessed from ACER (Average Cost-effectiveness Ratio) and ICER (Incremental Cost-effectiveness Ratio). The results showed that the effectiveness of antibiotics based on the clinical outcome temperature and length of cefazolin of 81.3% and 2.7 days while in clindamycin by 18.8% and 1.8 days. The ACER (Average cost effectiveness ratio) based on the clinical output of body temperature in both groups was IDR 64,348 (cefazolin) and IDR 98,319 (clindamycin). ACER values based on long of stay (LOS) clinical discharge in both groups amounted to IDR 19,375 (cefazolin) and IDR 10,268 (clindamycin). The value of ICER (Incremental Cost-effectiveness Ratio) cefazolin against clindamycin based on the clinical output of temperature and length of hospitalization (LOS) respectively is IDR 54,129 and IDR 37,590 for each effectiveness achieved. The conclusion of this study is that the use of cefeazoline is more therapeutically effective than clindamycin with greater therapeutic costs.

1. INTRODUCTION

Postpartum infection is a condition that occurs when bacteria enter and infect the uterus and the surrounding area after a woman gives birth either vaginally or by cesarean section. This infection is usually characterized by an increase in temperature to 38 degrees Celsius or more during the first 2-10 days postpartum. Infection occurs when microorganisms grow in body tissues, especially those that cause injury to body tissues and antibiotic therapy is required to overcome them (Prasanti, 2017).

The CDC (Center of Disease Control and Prevention) estimates that 84% of postoperative patients are diagnosed with the postoperative infection (Dudeck et al, 2013). Postpartum infection can increase anxiety in the mother and increase the risk of postpartum depression (Boushra and Rahman, 2015). The World Health

Organization (WHO) recommends that the prevention of postpartum infection is to provide prophylactic antibiotic therapy. However, inappropriate use of antibiotics can actually increase the risk of infection (World Health Organization, 2015). The increase in the incidence of postnatal infection in addition to increasing patient mortality and morbidity can also increase the burden of costs that must be paid by the patient. This increase in cost can be caused by an increase in the length of stay of patients in the hospital (Elattar, Selamat, Robson & Loughney, 2008).

Pharmacoeconomic studies have always been an important consideration due to limited resources, especially funds (Kementerian Kesehatan Republik Indonesia, 2013). Cost-Effectiveness Analysis (CEA) is one step to assess the comparison of health benefits and the resources used in health care programs and policymakers in choosing between alternatives. The results of the CEA are described as a ratio, either by an Average Cost-Effectiveness Ratio (ACER) or as an Incremental Cost-effectiveness Ratio (ICER). ACER represents the total cost of a program or alternative divided by the clinical outcome. The most cost-effective alternative is not always the one that costs the least to achieve a specific therapeutic goal. In this case, cost-effectiveness is not the cheapest cost but cost optimization (Andayani, 2013).

In a study conducted in India, the most widely used antibiotics in normal delivery were cephalosporin, followed by penicillin combination antibiotics with extended-spectrum penicillin. In cesarean delivery, the most frequently used antibiotics are third-generation cephalosporin (Sharma et al., 2013). Admaja, Herowati & Andayani (2019), concluded that cefazolin has a greater effectiveness value and a smaller ACER value than amoxicillin.

This study aims to determine the effectiveness of therapy and the cost of antibiotic therapy with cefazolin and clindamycin in postpartum patients at PKU Muhammadiyah Hospital, Yogyakarta. The benefits of this research are that it can add experience and knowledge for both researchers and students regarding the financing of clindamycin and cefazolin antibiotic therapy in postnatal patients at PKU Muhammadiyah Yogyakarta Hospital and for the community to find out how much the cost of antibiotic therapy for postpartum patients and what antibiotics are used. for postpartum patients.

2. RESEARCH METHODS

This study used a non-experimental (observational) research design with retrospective cohort data collection. The effectiveness of antibiotic therapy was measured based on the results of collecting patient medical record data and laboratory data in the form of measuring temperature and length of stay (LOS), while medical costs were directly obtained from the hospital finance department. Cost-effectiveness was assessed based on the ACER (Average Cost-Effectiveness Ratio) and ICER (Incremental Cost-Effectiveness Ratio) values during January-December 2020 period. The population in this study was an affordable population, namely postnatal patients who were hospitalized and received Cefazolin and Clindamycin therapy at the hospital. PKU Muhammadiyah Yogyakarta in 2020. The research subjects were taken by non-random or purposive sampling. The sample in this study was part of the population that met the inclusion criteria, namely postpartum patients who used the antibiotics Cefazolin and clindamycin and patients aged >20 years old. The exclusion criteria in this study were the patient died, the patient data was incomplete, the patient had other infections, and the patient had complications.

Research data derived from medical records include patient identity, education, decrease in the patient's average temperature, leukocyte values, and direct medical costs of patients obtained from the hospital administration. Medical costs consist of drug costs for postnatal patients, doctor services fees, costs hospitalization, laboratory examination fees, nursing service costs, and action costs. The tool used in this study was a data collection sheet (Lempar Pengumpul Data (LPD)) which contains patient demographic data, patient vital sign data, leukocyte examination, and patient treatment costs. In this study, outcomes were measured using temperature parameters and length of stay (LOS).

Research was preceded by obtaining a research permit and obtaining ethical clearance. Research permits were submitted to PKU Muhammadiyah Yogyakarta Hospital from December 2020 to June 2021. Ethical clearance is submitted to PKU Muhammadiyah Yogyakarta Hospital online through the website http://sim-epk.keppkn.kemkes.go.id. After obtaining research permits and ethical clearance, the researchers conducted a preliminary study to determine the number of postpartum patients at PKU Muhammadiyah Yogyakarta Hospital

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from January-December 2020. The purpose of the preliminary study was to determine the total population of postpartum patients receiving antibiotics.

The next step, the researcher took data to the hospital medical record section accompanied by a research supervisor (from the hospital) with ICD 080 (normal childbirth), 081 (vacuum childbirth), 082 (cesarean childbirth), 083 (breech childbirth), 084 (twin delivery). The medical record section will prepare patients who meet the criteria according to the ICD. From the medical record section, researchers are given a medical record number and registration number from January-December 2020. The medical record number is used to view patient data such as age, diagnosis, disease history, patient objective data, drug use data and patient cost data. Medical record data is viewed through EMR (Electronic Medical Record). Furthermore, after the data is obtained, the patients who meet the inclusion and exclusion criteria will be the subjects of this study. The therapeutic outcome measured in this study was a decrease in the patient's body temperature and length of stay. Therapy is effective if the patient does not have a fever (body temperature <37.5 °C).

Data analysis conducted in this research is descriptive. Then the ACER (Average Cost-Effectiveness Ratio) and ICER (Incremental Cost-Effectiveness Ratio) values were calculated.

3. RESULTS AND DISCUSSIONS

This research has received Ethical Clearance permission from the ethics committee of PKU Muhammadiyah Yogyakarta Hospital number: 00035/SRIP/KEP-PKU/XI/2020. Based on observations from December 2020-March 2021 and taking patient data from medical records in the January-December 2020 period, there were 362 who gave birth and received treatment at PKU Muhammadiyah Yogyakarta Hospital. Subjects used were 65 hospitalized patients, 39 taking cefazolin antibiotics, and 26 clindamycin had inclusion criteria. Meanwhile 292 patients were excluded, 43 patients were not taking antibiotics, 187 patients were taking other antibiotics and 68 patients had incomplete medical and financial records.

Most of the research subjects were aged 27-32 years with a percentage value of 38.46% for cefazolin and 38.5% for clindamycin (**Table 1**). The best age for giving birth is 20-35 years. Women who become pregnant at an age too young (<20 years old) or too old (>35 years old) are at higher risk for complications of childbirth and pregnancy (Salim, Sukarya & Hikmawati, 2015).

The average gestational age in the cefazolin group was 35-38 weeks, while in the clindamycin group, the largest gestational age was 27-32 weeks. A normal pregnancy will take place within 36-40 weeks. Pregnancy takes place in three semesters (trimester). The first trimester takes place in the first 13 weeks, the second trimester starts at the 14th week to the 27th week, and the third trimester starts from the 28th to the 40th week (Yanti, 2015). WHO classifies births based on gestational age, namely term births and premature births. Term births if births occur at more than 37 weeks of gestation, while premature births if births occur at less than 37 weeks of gestation. This premature birth can increase the risk of death in infants and cause health problems in infants including respiratory problems, cerebral palsy, stunted growth, visual, and hearing impairments (Center of Disease Control and Prevention, 2021).

Table 1. Characteristics of Postpartum Patients at PKU Muhammadiyah Hospital Yogyakarta

Patient Characteristics		Antibiotics		p (sig)
		Cefazolin (n=39) (amount=%)	Clindamycin (n=26) (amount=%)	
Age	20-26 years old	10 (25,64 %)	7 (27 %)	0,999
	27-32 years old	15(38,46 %)	10(38,5 %)	
	33-38 years old	11(28,2 %)	7(27 %)	
	>38 years old	3(7,7 %)	2(7.5 %)	
Gestational Age	31-34 weeks	4(10,26 %)	3(11,54 %)	0,519
	35-38 weeks	24(61,54 %)	14(53,85 %)	
	39-42 weeks	9(23,1 %)	9(34,62 %)	
	>42 weeks	2(5,13 %)	0	
Diagnosis	Normal Childbirth	10(25,64 %)	26(100,0%)	*0,000
	Vacuum Childbirth	2(5,12%)	0	
	cesarean childbirth	27(69,24%)	0	

obtained using the Chi-Square. Test
p-value <0.005 indicates there is a significant difference

Table 2. Use of Antibiotics in Postpartum Patients at PKU Muhammadiyah Hospital Yogyakarta

Antibiotics	Amount (n=65)	%
Cefazolin	39	60%
Clindamycin	26	40%

Table 3. Drug Use in Postpartum Patients at PKU Muhammadiyah Hospital Yogyakarta

No	Drug	Content of drug	Cefazolin		Clindamycin	
			n=39	%	n=26	%
1	Vitamin A	Vitamin A	26	66,67	20	76,92
2	supplement	vitamin B Complex	5	12,82	1	3,85
		Vitamin C	11	28,21	1	3,85
		Dietary supplement	2	5,13	8	30,77
		Iron	5	12,82	1	3,85
		Calcium Lactate	0	0,00	1	3,85
		Mg Sulfat 20%	2	5,13	1	3,85
3	Methylergometrine	Methylergometrine	13	33,33	37	142,31
4	Lidocaine	Lidocaine	1	2,56	8	30,77
5	Anti-ulcer	Lansoprazole	5	12,82	5	19,23
6	Oxytocin	Oxytocin	13	33,33	20	76,92
7	Misoprostol	Misoprostol	5	12,82	9	34,62
8	Analgesic	Mefenamic acid	23	58,97	22	84,62
		Tramadol	7	17,95		0,00
		Tramadol +acetaminophen	3	7,69		0,00
		Acetaminophen	1	2,56	3	11,54
9	Anti-inflammatory	Dexamethasone	4	10,26	1	3,85
		Pronalges® Suppository	2	5,13		0,00
		Ketorolac	12	30,77		0,00
10	Antihypertensive	Nifedipine	3	7,69		0,00
		Dopamet®	3	7,69	1	3,85
		Adalat Oros®	4	10,26		0,00
		Captopril	2	5,13		0,00
		Furosemide	1	2,56		0,00
11	Ringer Lactate	Ringer lactate	4	10,26	5	19,23
12	Anti-hemorrhagic		1	2,56		0,00

In this study, the majority of patients receiving cefazolin delivered cesarean delivery, followed by vaginal and vacuum deliveries. In contrast to the clindamycin group, all patients delivered vaginally. This is in accordance with the guidelines for the use of antibiotics, where at cesarean childbirth the purpose of using antibiotics is as prophylaxis, with the first choice being cefazolin. Meanwhile, in normal premature births, giving prophylactic therapy with clindamycin (World Health Organization, 2015).

The antibiotics used by postnatal patients at PKU Muhammadiyah Yogyakarta Hospital were cefazolin as much as 39 with a percentage of 60% and clindamycin 26 with a percentage of 40% (**Table 2**). This study is in line with a study by Sharma et al., (2013), which showed that most of the antibiotics prescribed to patients postpartum is a third-generation cephalosporin.

Vitamin C in patients using the antibiotic cefazolin was 28.21% and clindamycin 3.85% while for iron tablets, cefazolin was 12.82% and clindamycin was 3.85%. The use of vitamin B complex in the use of cefazolin antibiotics was 12.82% and for clindamycin 3.85%. The use of other drugs such as methylergometrine for the use of clindamycin antibiotics were 142.31% and for cefazolin were 33.33%. The use of oxytocin in the clindamycin group was 76.92% and in the cefazolin group was 33.33%. The misoprostol was used by patients taking clindamycin (34.62%) and cefazolin (12.82%). Misoprostol is used as a drug for labor induction, so the FDA has given a new label for the use of misoprostol in pregnancy because it is able to make cervical ripening and stimulate myometrial contractions (Cunningham et al., 2013). The use of lidocaine in patients taking clindamycin was 30.77% and cefazolin was 2.56%. The use of antiulcer drugs in clindamycin was 19.23% while cefazolin was 12.82%. Research on the description of drug use in Post-SC patients in Magelang showed that most of the patients received antibiotics, followed by painkillers, multivitamins, cough medicines and allergy medicines. (Irwansyah 2020).

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Table 4. Comparison of the effectiveness of cefazolin and clindamycin antibiotic therapy based on body temperature at PKU Muhammadiyah Hospital Yogyakarta

Effectiveness	Cefazolin (n=39)	Clindamycin (n=26)	p (sig)
Effective	26 (81.3%)	6 (18.8%)	0,001*
Ineffective	13 (39.4%)	20 (60.6%)	

Table 5. Therapeutic effectiveness in postpartum patients at PKU Muhammadiyah Hospital Yogyakarta based on Length of Stay (LOS)

Antibiotics	Minimum Hospitalization (Days)	Maximum Hospitalization (Days)	Average (Days)	P
Cefazolin	1	5	2,7	0,001*
Clindamycin	1	5	1,8	

*The p-value indicates a significant difference between the two groups (p<0.005)
The p value was obtained from the Chi-Square test

Effectiveness of therapy based on body temperature

The effectiveness of this study was measured using two clinical outcomes. The first clinical outcome is the patient's body temperature. The number of patients who used the more effective antibiotic cefazolin was 81.3% while clindamycin was 18.8% (Table 4). The effectiveness of the use of antibiotics was assessed based on the decrease in the patient's body temperature until it reached a normal value (<37.5 °C) during hospitalization. From the results of therapy, it was seen that cefazolin had more therapeutic effectiveness, namely 26 patients while clindamycin was only 6 patients. The p value of 0.001 (<0.05) indicates a statistically significant difference in the effectiveness of the two antibiotics based on the patient's body temperature.

Research conducted to see the effectiveness of antibiotic therapy in post-cesarean patients showed that most of the therapies were said to be effective based on the clinical outcome of the patient's recovery (Prasetya, 2013). Another study on the effectiveness of antibiotic therapy after cesarean childbirth by Hardiyanti, Rosdiani, Kurniawati & Sari (2020), showed that based on the effectiveness of reducing the temperature, patients receiving prophylactic antibiotic therapy had a normal average temperature (36-36.6 °C). This shows that post-cesarean antibiotic therapy can prevent post-delivery infection.

Effectiveness of therapy based on length of stay

Length of stay is calculated from the time the patient enters the hospital until the patient leaves the hospital. Postpartum patients who received cefazolin had an average length of stay of 2.7 days, while patients treated with clindamycin had an average of 1.8 days (Table 5). Based on the chi-square analysis, the results of the p value = 0.001 (<0.05) can be interpreted as a significant difference in the outcome of the patient's length of stay.

Hardiyanti (2020), also conducted an effectiveness analysis based on the length of hospitalization. Based on this research, it is known that the length of stay for post-cesarean patients receiving antibiotic therapy is three to four days. Another study comparing the effectiveness of cefazolin therapy with clindamycin or metronidazole in patients at risk for postpartum infection showed that cefazolin was more effective than clindamycin or metronidazole. Administration of cefazolin gave a smaller odds ratio concerning the incidence of postpartum infection (Venkatesh et al. 2020).

Cost Analysis

Cost analysis in this study uses a hospital cost perspective. Direct costs are related to direct patient care, such as drug costs, doctor fees, laboratory test fees (Kementerian Kesehatan RI, 2013). The direct medical costs in this study consisted of six types of payments: the cost of antibiotics, the cost of drugs and medical devices, the cost of supporting examinations, inpatient care, administration fees, and doctor fees. The following is a recapitulation of postnatal patient costs at PKU Muhammadiyah Yogyakarta Hospital.

The highest direct treatment costs are the treatment costs for patients using the antibiotic cefazolin, which is IDR 6,983,425. and the lowest total direct treatment costs were patients who used clindamycin antibiotic therapy, which was IDR 2,996,905 (Table 6). Cost-effectiveness analysis was measured using ACER (Average Cost-effectiveness Ratio) and ICER (Incremental Cost-effectiveness Ratio) values. ACER is calculated based on the average total medical cost of antibiotics during treatment divided by the effectiveness of therapy (%). ICER is calculated based on the difference in the average total cost of antibiotics for drug A and drug B divided by the difference in the effectiveness of drug A and drug B.

Table 6. Average Drug Costs for Postpartum Patients at PKU Muhammadiyah Hospital Yogyakarta

Payment Name	Cefazolin (n=39)	Clindamycin(n=25)
Antibiotic Cost	IDR 52,315	IDR 18,484
Cost of Medicine and Medical Devices	IDR 1,864,282	IDR 550,121
Supporting Examination Fee	IDR 768,979	IDR 524,903
Inpatient Treatment Cost	IDR 1,222,217	IDR 947,919
Administrative costs	IDR 86,512	IDR 88,203
Doctor Fee	IDR 3,041,433	IDR 885,716
Total Average	IDR 6,983,425	IDR 2,996,905

Table 7. ACER Calculation for Postpartum Patients at PKU Muhammadiyah Hospital Yogyakarta

Types of Antibiotics	Average Cost of Antibiotics	Effectiveness		ACER Value	
		Temperature	LOS	Temperature	LOS
Cefazolin	IDR 52,315	81.3%	2,7	IDR 64,348	IDR 19,375
Clindamycin	IDR 18,484	18.8%	1,8	IDR 98,319	IDR 10,268

Table 8. ICER calculation based on clinical outcomes of length of stay and temperature in postpartum patients at PKU Muhammadiyah Hospital in Yogyakarta

Antibiotics	Cost (IDR)	Effectiveness	ICER (IDR)
Outcome of Temperature			
Cefazolin	52,315	0,813	54,129
Clindamycin	18,484	0,188	
Outcome of LOS			
Cefazolin	52,315	2,7 days	37,590
Clindamycin	18,484	1,8 days	

The ACER value based on the temperature output is IDR 64,348 (cefazolin) and IDR 98,319 (clindamycin) (Table 7). This ACER value indicates that the use of cefazolin is more cost-effective than clindamycin. Admaja et al., (2019), showed that cefazolin has higher effectiveness with a lower ACER value than amoxicillin in cesarean section patients. This indicates that the results of this study are in line with previous studies. The ACER value for the LOS was IDR 19,375 for cefazolin and IDR 10,268 for clindamycin (Table 7). This means that clindamycin has lower cost-effectiveness than cefazolin based on LOS. Research conducted by Admaja et al., (2019), regarding the cost-effectiveness of prophylactic antibiotics in post-surgical patients showed that cefazolin had a lower ACER value than amoxicillin, which was IDR with amoxicillin.

The ICER value from comparing the cost difference with the effectiveness of LOS on cefazolin and clindamycin antibiotic therapy is IDR 37,590, which means that the additional cost of cefazolin and clindamycin for the clinical outcome of LOS in postpartum patients is IDR 37,590 (Table 7). The result between the cost difference and the price difference between cefazolin and clindamycin antibiotic therapy is IDR 54,129 (Table 7), which means that the additional cost of cefazolin to clindamycin for the clinical outcome of temperature in postpartum patients is IDR 54,129.

4. CONCLUSION

Based on the clinical outcome of temperature, cefazolin has a lower ACER value than clindamycin but based on the outcome of hospitalization, clindamycin has a lower ACER value. Based on ICER calculations on temperature output, it shows that cefazolin requires an additional cost of IDR. 54,129 for each temperature reduction achieved, and cefazolin requires an additional cost of IDR 37,590/day.

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