RATIONALITY OF ANTIBIOTICS USE WITH QUANTITATIVE AND QUALITATIVE METHODS AT HOSPITAL IN INDONESIA

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Abstract

Infection is one of the biggest causes of death in Indonesia which can be influenced by the appropriate use of antibiotics. Irrational use of antibiotics can cause bacteria to become resistant to antibiotics so that the effectiveness of the drug decreases or even disappears. This study aims to evaluate the use of antibiotics given to inpatients at a private hospital in Indonesia both quantitatively and qualitatively in the period July to December 2021. This study is an observational study with retrospective data collection where qualitative analysis using the Gyssens Method and quantitative analysis uses the DDD method. The results of the qualitative analysis showed that from 30 cases observed, there were 9 cases (30%) irrational prescriptions, namely 1 case in category V, 4 cases in category IVA, 2 cases in category IIIB and 2 cases in category IIA. The results of the quantitative analysis showed that the antibiotics with the highest DDD/100 patient days in the period July to December 2021 were Ceftriaxone with a successive value of 39.15; 39.81; 36.22; 55.65; 41,48 and 49, 42 while antibiotics with the lowest DDD/100 patient-days values in the period July to December obtained different results. Based on research results, there are irrational antibiotic prescriptions and Ceftriaxone became the most commonly prescribed antibiotic.

Keywords: A*ntibiotics, DDD Method, Gyssen Method*

1. INTRODUCTION

Infection is a health problem that is one of the causes of death and illness in hospitals and other health care facilities in Indonesia. Antibiotics are the drug of choice used to treat infectious diseases. Antibiotics are chemical substances produced by bacteria that have the property of inhibiting or killing bacterial growth (Tjay & Rahardja, 2007). The use of antibiotics in patients should pay attention to the time, dose and duration of administration according to the therapeutic regimen as well as patient compliance with the use of antibiotics, if this is neglected it can be at risk of causing bacteria resistant to antibiotics (Indonesian Ministry of Health, 2011).

Resistance occurs when bacteria are no longer sensitive to the action of antibiotics or antibiotics are unable to eradicate bacteria due to loss of drug effectiveness. Bacterial resistance to antibiotics, especially if multi-drug resistance is a problem that will be difficult to overcome. Several studies show that the irrational use of antibiotics is around 20% - 50% while for the use of antibiotics that are not based on indications as much as 18% - 40% (Novianae, 2020). When the patient is already resistant to an antibiotic, then another antibiotic that is more effective must be chosen so that infectious diseases can be treated properly.

Experts say that we are currently approaching the post-antibiotic era, a condition where antibiotics are no longer useful for treating an infection and the prevalence of antibiotic resistance is increasing. This will easily damage public health conditions. Again, this resistance occurs due to irrational antibiotic prescribing which can later have an impact on increasing treatment costs, length of hospital stays and increased mortality. So that in the end it is necessary to evaluate the use of antibiotics both quantitatively and qualitatively so that inappropriate or irrational use of antibiotics does not occur (Samuel, 2019). Indonesia itself, has general guidelines for the use of antibiotics in the regulation of the Minister of Health of the Republic of Indonesia number 2406/MENKES/PER/XII/2011. These guidelines aim as a reference for health workers in using antibiotics and there are principles of preventing antibiotic resistance (Ministry of Health Regulation, 2011).

2. LITERATURE REVIEW

Antibiotics are the drug of choice used to treat infectious diseases. Antibiotics are chemical substances produced by bacteria that have the property of inhibiting or killing bacterial growth (Tjay & Rahardja, 2007). Irrational or inappropriate use of antibiotics will cause bacteria to become resistant to antibiotics, antibiotics are the most widely used drugs for infections caused by bacteria. Various studies have found that about 40-62% of antibiotics are used inappropriately, among others, for diseases that do not actually require antibiotics. (Indonesian Ministry of Health, 2011).

Bacterial resistance to antibiotics, especially if multi-drug resistance is a problem that will be difficult to overcome. Based on data from Antimicrobial Resistance: Global Report on Surveillance, Southeast Asia is the country with the highest antibiotic resistance cases in Asia. The increase in the incidence of bacterial resistance to antibiotics can occur by two mechanisms. First, with the Selection Pressure mechanism, when these resistant bacteria multiply in duplication every 20-30 minutes (for bacteria that reproduce quickly), then within 1-2 days, a person is filled with resistant bacteria. If a person is infected with resistant bacteria, it will be more difficult to treat the infection with antibiotics. Prevention of the increase in antibiotic resistance with the Selection Pressure mechanism is through the prudent use of antibiotics. The second mechanism is the spread of resistance to non-resistant bacteria through plasmids. It can be spread between a group of germs or from one person to another. The spread of resistant bacteria through plasmids can be overcome by increasing adherence to the principles of standard precautions (universal precautions) (Indonesian Ministry of Health, 2011).

The use of antibiotics can be evaluated qualitatively and quantitatively. Qualitatively, antibiotics were evaluated using the Gyssens method. This method is used to assess the appropriateness of the use of antibiotics, based on grouping categories 0 to 6 based on the accuracy of the indication, the accuracy of the selection based on effectiveness, toxicity, price and spectrum, duration of administration, dose, interval, route and time of administration. The Gyssens method is a tool to evaluate the quality of the use of antibiotics that have been widely used in various countries (Gyssens, 2005).

Quantitatively, antibiotics were evaluated using the DDD or Defined Daily Dose method. This method is carried out by calculating the DDD used per 100 patient-days which

aims to evaluate the type and amount of antibiotics used. The choice of quantitative evaluation with this method is also because it can be used to compare the quantity of antibiotic use between hospitals and between countries. Therefore, the results of this study can be used as a comparison of the amount of antibiotic use in other places with the same method and calculation. In the ATC system, drugs are divided into different groups based on the organ or system in which they act as therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five different levels. DDD is assumed to be the value of the average daily maintenance dose used for the main indication in adults. The DDD System is an Assessment of the Quantity of Antibiotic Use Quantity of antibiotic use is the amount of antibiotic use in a hospital which is measured retrospectively and prospectively through a validation study (Indonesian Ministry of Health, 2011).

3. RESEARCH METHOD

This study is an observational study with retrospective data collection. The study was conducted at one of the private hospitals in Indonesia on July - December 2021.

### a. Inclusion and exclusion criteria

The analysis was carried out qualitatively and quantitatively. The inclusion criteria from the qualitative analysis were inpatients who received oral and parenteral antibiotic therapy with a diagnosis of neurological, cardiac, internal, surgical and pediatric patients, while the exclusion criteria were the use of take-home antibiotic therapy and incomplete medical records. The inclusion criteria from the quantitative analysis were hospitalized patients who received oral and parenteral antibiotic therapy, while the exclusion criteria were the use of take-home antibiotic therapy.

b. Data collection techniques

Sampling was done by purposive sampling technique, namely taking samples that meet the inclusion criteria within the specified time span.

c. Data collection and analysis

The data used for the qualitative analysis was taken from the patient's medical record data in several predetermined cases. Evaluation of the quality of antibiotic use is based on the Gyssens flow chart, then the results are stated in categories, namely 0-VI (Gyssens, 2005). The following is the flow of the Gyssens Diagram:
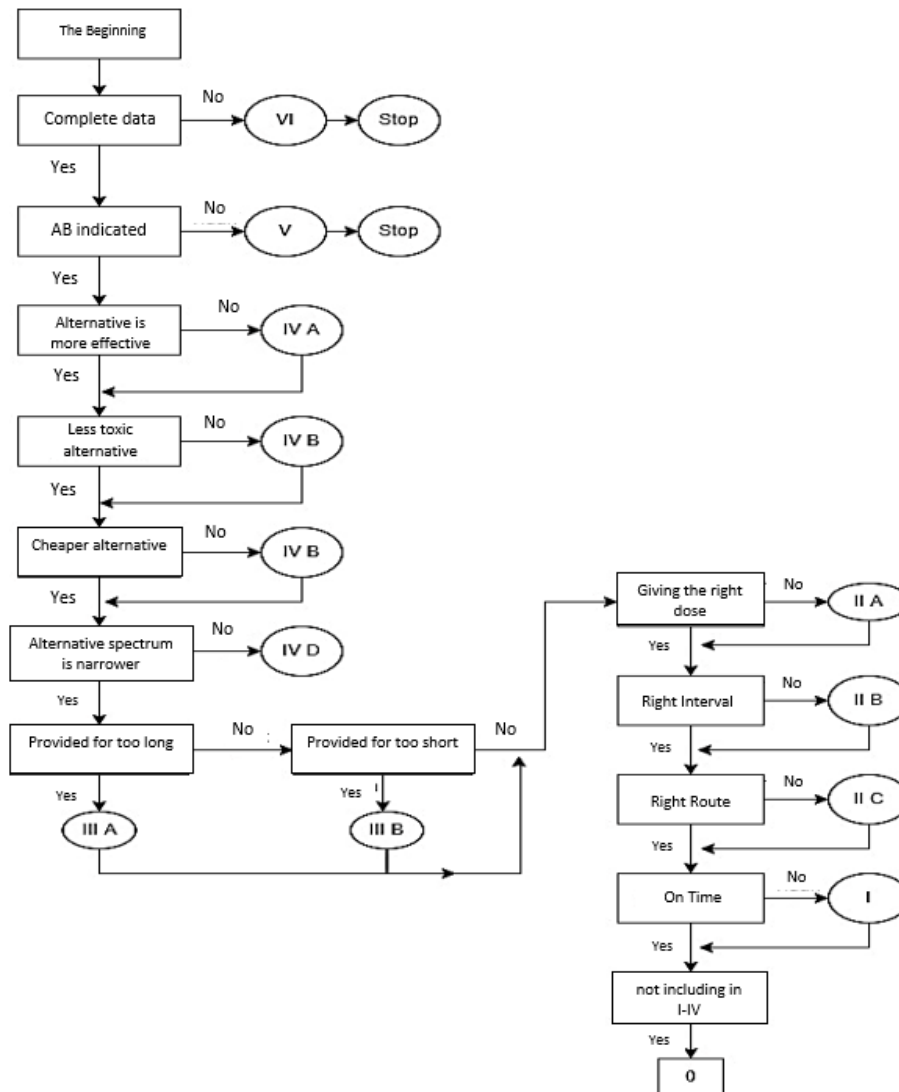
Figure 1 Gyssens Flow

Data for quantitative analysis is taken from the request and administration card (KPPO) while the patient is hospitalized. Quantitative analysis of antibiotics uses the ATD/DDD method and is calculated by the following formula:

$$DDD/100\ patient - days = \frac{\text{The amount of AB the patient uses}}{\text{Standar DDD WHO}} \times \frac{100}{\text{total LOS}}$$

The number of antibiotics and WHO DDD standards are expressed in grams (Indonesian Ministry of Health, 2011). Processing results and quantitative and qualitative processed using Microsoft Excel software, then the results of the calculations are converted into percentages and presented in tabular form.

4. RESULT AND DISCUSSION

In this study, quantitative and qualitative evaluation of antibiotics was carried out. Quantitative evaluation using the DDD method, data obtained from KPPO data for July - December 2021, while qualitative evaluation using the Gyseens method where data were obtained from 30 medical record data (internal medicine, heart, neurology, surgery, obstetrics and gynecology, and children) respectively in 5 poly cases.

4.1. Qualitative Method

Qualitative evaluation using 30 cases of prescribing antibiotics in patients undergoing inpatient treatment at a hospital in Indonesia during the period July - December 2021. Antibiotic prescribing cases were evaluated using a Gyssen flow chart and then classified by Gyssens category in the range Category VI – 0 (Gyssens, 2005). The results of the evaluation of antibiotic prescribing in this study can be seen in the following figures:
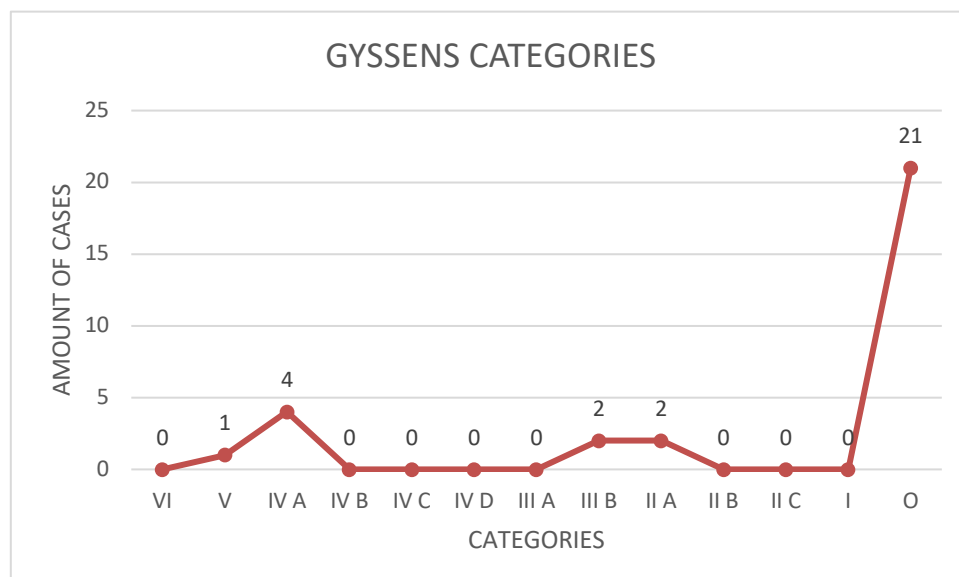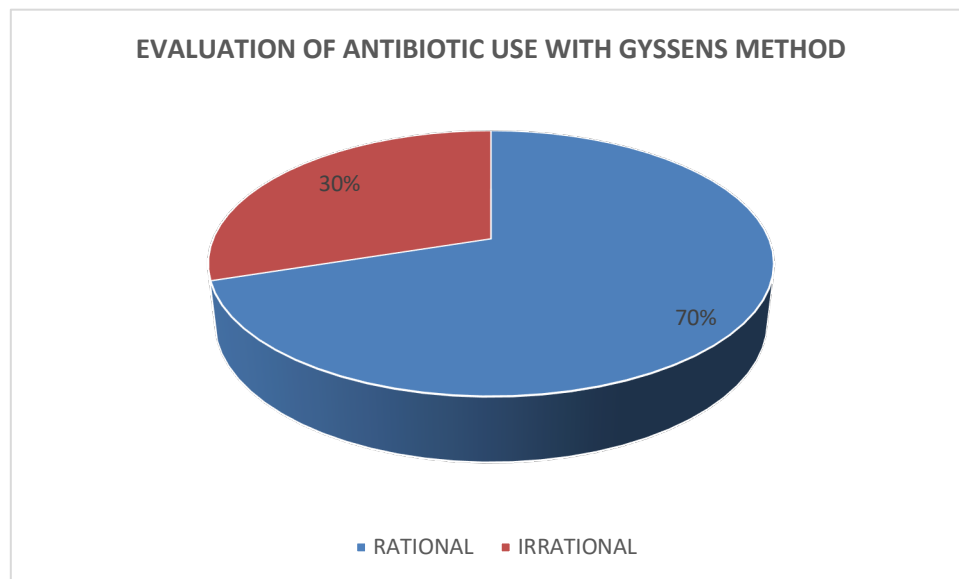

Figure 2 Gyssen Method Antibiotic Evaluation Results

Figure 3 Percentage of Antibiotic Rationality

Of the 30 cases used as sample data in this research, there were a total of 9 cases in which the administration of antibiotics could be said to be irrational. The 9 cases were divided into three gyssen categories, namely 1 case in category V (no indication for antibiotics), 4 cases in category IV A (There are more effective antibiotics), 2 cases were in category III B (Use of antibiotics was too short) and two cases were in category II A (antibiotics were not dosed correctly). Irrational antibiotics occur mostly in category IV A and in case 16 they fall into two categories, namely III B and II A.

In the case of 20 patients with a diagnosis of anterior stem received ciprofloxacin antibiotic therapy. However, in these patients, laboratory data for leukocyte numbers showed normal values, there was no urine bacterial culture in the urinalysis test. In addition, the clinical condition of the patient also did not show symptoms of infection so that the administration of antibiotics was not appropriate.

In case 1, a patient with suspected tuberculosis was treated with ceftriaxone and azithromycin. According to the Guidelines for Treatment of Drug-Suspectible Tuberculosis and Patient Care, it is recommended that antibiotic therapy in patients with suspected tuberculosis use the standard therapy regimen for tuberculosis therapy, namely 2HRZE/4HR, but macrolide antibiotic prescribing has previously been used in the treatment of multidrug-resistant tuberculosis (WHO, 2020). Case 1 is included in the IVA category because 2HRZE/4HR is more effective in the treatment of tuberculosis when compared to centriaxone and azythromycin.

In case 11, an adult patient with a diagnosis of Diabetes mellitus with pedis ulcer received antibiotic therapy with ceftriaxone injection. According to the guidelines for Diabetic foot problems: Prevention and Management, the recommended antibiotics for moderate to severe foot infections aged 18 years and over are flucloxacillin alone or in combination, gentamicin alone or in combination with metronidazole, co-amoxiclav with or without gentamicin, co-trimoxazole (if penicillin allergy) with or without gentamicin, or when using ceftriaxone in combination with metronidazole (NICE, 2015). Thus case 11 is

also included in the IVA category because there are other, more effective antibiotics to choose from.

In the case of 13 patients with a diagnosis of FAM dextra with signs of abscess infection received cefotaxime antibiotic therapy. According to the guidelines for the Management of Lactational Mastitis and Breast Abscesses, the Review of Current Knowledge and Practice recommends the penicillin group, because penicillin is acidic so its concentration in breast milk is not much because it is also acidic, so erythromycin can be given because resistance to staphylococci strains is still rare. However, if the patient is allergic to penicillin, cefalexin or clindamycin, an alternative that can be used is erythromycin (Kataria et al., 2013). Thus case 13 is included in the IVA category because penicillin is more recommended than cefotaxime.

In the case of 18 patients with a diagnosis of ischemic heart disease with signs of infection seen from an increase in the number of leukocytes and prescribed antibiotic therapy ciprofloxacin. Meanwhile, according to Antibiotics for Secondary Prevention of Ischemic Heart Disease, recommends the macrolide group, namely azhithromycin, chlaritomycin, and roxithromycin because infection is suspected as part of the pathogenesis of ischemic heart disease which is usually caused by Chlamydia pneumoniae where these bacteria correlate with the risk of myocardial infarction (Wells et al., 2004). Thus case 18 was included in the IVA category because the macrolide group was more recommended than ciprofloxacin.

Furthermore, there were two cases that were included in category III B (the duration of antibiotic administration was too short), namely cases 16 and 19. In case 16, the patient had COPD and received Ciprofloxacin therapy for 4 days. Based on the literature, antibiotic therapy for COPD is given for 7-10 days (DiPiro et al., 2015). In case 19, the patient had a UTI and was treated with Ciprofloxacin for 4 days. Based on the literature, UTI therapy for the mild to moderate category is given for 7-14 days (American Society of Health System Pharmacists, 2011).

Lastly, there were two cases that were included in category II A, namely cases 16 and 19. In case 16, the patient had COPD and was treated with Ciprofloxacin 2 x 200 mg. Based on the literature, the dose of antibiotic therapy for COPD is 2 x 500 mg (American Society of Health System Pharmacists, 2011). In case 28, the patient had acute diarrhea and was treated with Cefixime 2 x 2.25 ml. Based on the literature, the therapeutic dose of cefixime antibiotics for children is 4 mg/kg BW every 12 hours, so the recommended dose in this case is 2 x 2.6 ml (American Society of Health System Pharmacists, 2011).

4.2. Quantitative Method

This study was conducted to see the description of the quantity of antibiotic use in inpatients at a private hospital in Indonesia from July to December 2021. The results of data collection, obtained 3499 prescription sheets (KPPO) with 1562 sheets receiving antibiotics. The total use of antibiotics in July to December 2021, obtained 15 types of antibiotics namely Ceftriaxone, Vicillin, Cefotaxime, Metronidazole, Cefoperazone, Gentamicin, Ciprofloxacin, Ceftazidime, Amikacin, Levofloxacin, Rifampicin, Clindamycin, Azithromycin, Cefixime, and Amoxicillin.

The calculation results show that the antibiotic with the highest DDD/100 patient days value in the period July to December 2021 is Ceftriaxone with a successive percentage of

39.15; 39.81; 36.22; 55.65; 41.48 and 49.42. Antibiotics with the lowest DDD/100 patient-days values in the period July to December were different. In July with a value of 0.03 for Gentamicin antibiotics, In August with a value of 0.01 on Amoxicillin antibiotics, September with a value of 0.03 for Amikacin antibiotics, in October with a value of 0.01 on Amikacin antibiotics, in November with a value of 0.02 on the antibiotic Gentamicin, and in December with a value of 0.01 on the antibiotic Gentamicin.

The smaller the value of the antibiotic DDD produced, the better the quantity of antibiotic use. This shows that the selection and use of antibiotics is more selective in prescribing antibiotics so that it is closer to the principle of rational use of antibiotics (Rukminingsih & Apriliyani, 2021). Meanwhile, the most widely used antibiotic percentage from July to December was ceftriaxone with a percentage of 34.33%, respectively; 50.54%; 39.19%; 55.31%; 37.35%; 48.41%.

Ceftriaxone is a third-generation cephalosporin antibiotic. The frequency of use of ceftriaxone in the hospital is quite high in adults. The high frequency of use causes the compounding of ceftriaxone to be carried out in hospitals is also high. Ceftriaxone is an antibiotic that is often prescribed because it has a broad spectrum and is effective for the treatment of infections caused by gram-positive, negative and anaerobic bacteria (Rachmawati et al., 2020). In addition, Ceftriaxone also has a relatively cheap price and relatively less toxicity compared to other types of antibiotics (Ardyanti, 2016).
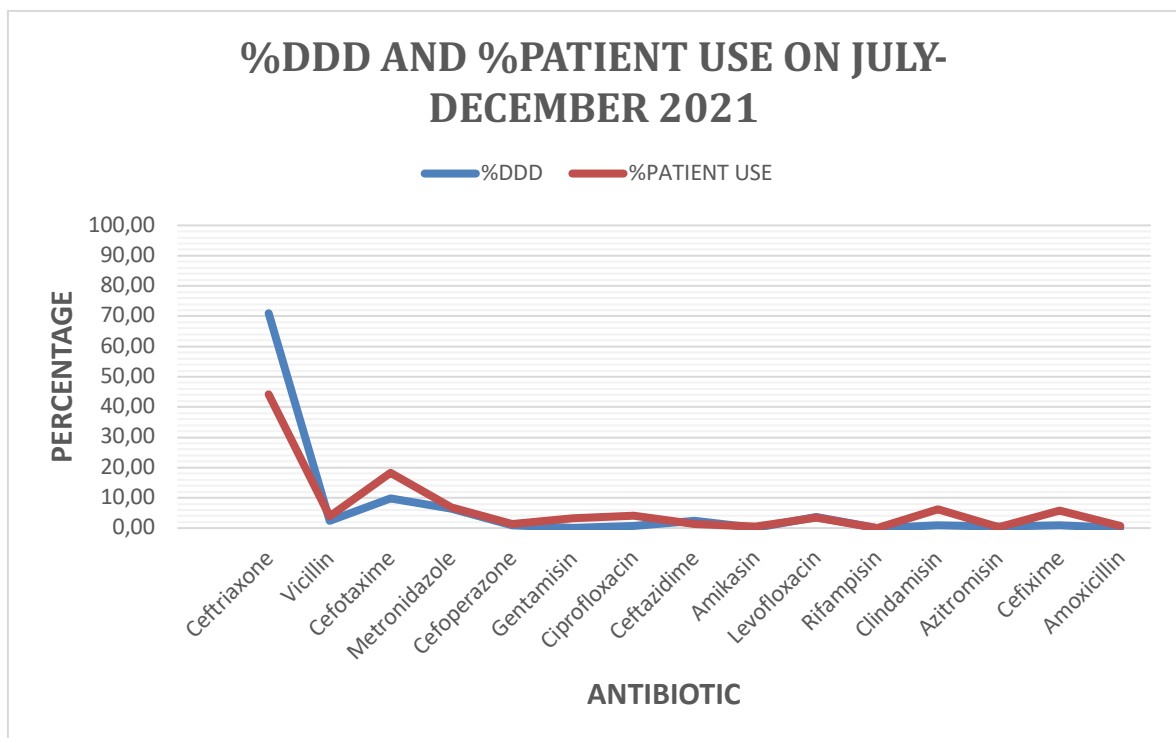
Figure 4 Results of Antibiotic Evaluation with the DDD Method

5. CONCLUSION

The rationale of antibiotics use was analyzed qualitatively and quantitatively. Qualitatively, antibiotics were analyzed using the Gyssens method in July to December 2021 with taking data by sampling, namely 30 cases of medical records. From these data, the accuracy of the indication, dose, route of administration, interval of administration and price of antibiotics was observed. The results obtained were that 70% of the use of antibiotics was appropriate/rational and 30% of antibiotic prescribing was still incorrect/irrational, while quantitatively, antibiotics were analyzed using the ATC/DDD method. The results show that from July to December 2021 there were 3499 prescription sheets (KPPO) with 1562 sheets receiving antibiotics. The most widely prescribed type of antibiotic was Ceftriaxone with an average percentage of 44,19%.

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